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Members of the Executive Committee of Associated Universities, Inc., at their first meeting on the site of Brookhaven National Laboratory, February 28. Left to right: Edward Reynolds, president of AUI and administrative vice-president, Harvard University; I. I. Rabi, executive officer, Department of Physics, Columbia University; J. R. Zacharias, professor of physics, Massachusetts Institute of Technology; P. S. Macaulay, provost, Johns Hopkins University; G. A. Brakeley, vice-president, Princeton University; and Philip M. Morse, director, Brookhaven National Laboratory (see *News and Notes*).

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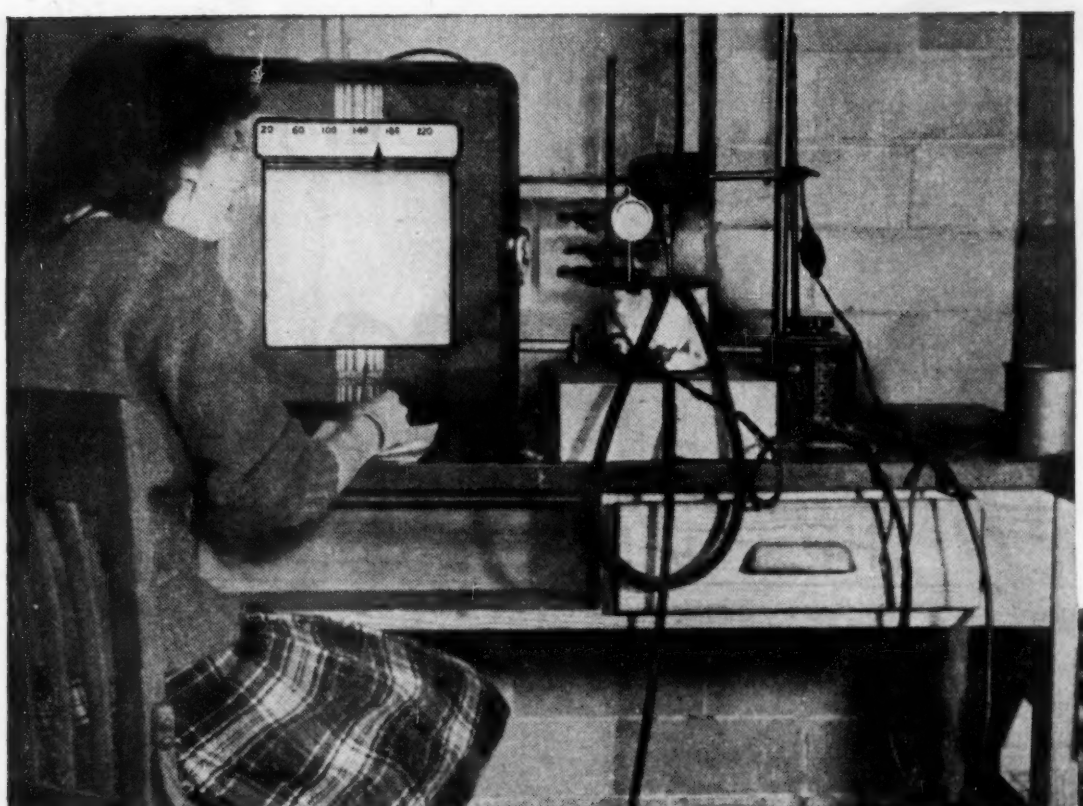
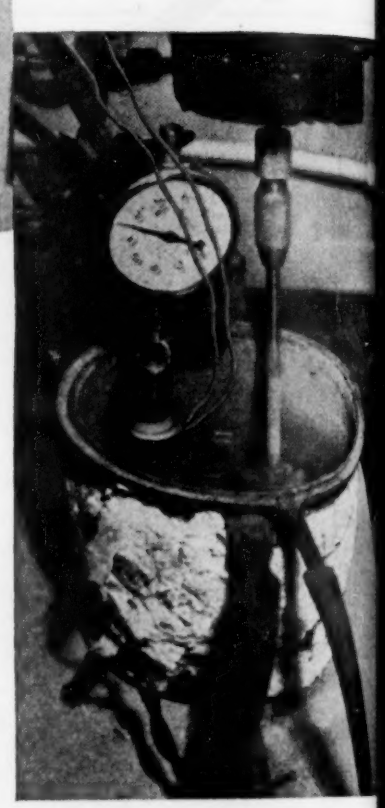
An American Bridge to World Science

William Vogt





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Science

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An American Bridge To World Science

William Vogt

2101 New Hampshire Avenue, N.W., Washington, D. C.

BOTH THE SCIENTIFIC AND THE GENeral press have been strangely neglectful of what is potentially a major opportunity to advance American science and, through it, to contribute to world peace. Indeed, there is considerable danger that, because of lack of action on the part of American scientific organizations, the opportunity may be sharply curtailed.

Senator J. William Fulbright introduced into the 79th Congress a bill to amend the Surplus Property Act of 1944. This bill, which was subsequently passed as Public Law 584, states in part:

> In addition to the authority conferred by section 15 of this Act, the Department of State may dispose of surplus property located outside the continental United States, Hawaii, Alaska (including the Aleutian Islands), Puerto Rico, and the Virgin Islands, for foreign currencies or credits, or substantial benefits or the discharge of claims resulting from the compromise, or settlement of such claims by any Government agency in accordance with the law, whenever the Secretary of State determines that it is in the interest of the United States to do so and upon such terms and conditions as he may deem proper. Any foreign currencies or credits acquired by the Department of State pursuant to this subsection shall be administered in accordance with procedures that may from time to time be established by the Secretary of the Treasury and, if and when reduced to United States currency, shall be covered into the Treasury as miscellaneous receipts.
>
> In carrying out the provisions of this section, the Secretary of State is hereby authorized to enter into an executive agreement or agreements with any foreign government for the use of currencies, or credits for currencies, of such government acquired as a result of such surplus property disposals, for the purpose of providing, by the formation of foundations or otherwise, for (A) financing studies, research, instruction, and other educational activities of or for American citizens in schools and institutions of higher learning located in such foreign country, or of the citizens of such foreign country in American schools and institutions of higher learning located outside the continental United States, Hawaii, Alaska (including the Aleutian Islands), Puerto Rico, and the Virgin Islands, including payment for transportation, tuition, maintenance, and other expenses incident to scholastic activities; or (B) furnishing transportation for citizens of such foreign country who desire to attend American schools and institutions of higher learning in the continental United States, Hawaii, Alaska (including the Aleutian Islands), Puerto Rico, and the Virgin Islands, and whose attendance will not deprive citizens of the United States of an opportunity to attend such schools and institutions: *Provided, however,* That no such agreement or agreements shall provide for the use of an aggregate amount of currencies, or credits for currencies, of any one country in excess of $20,000,000 or for the expenditure of the currencies, or credits for currencies, of any one foreign country in excess of $1,000,000 annually at the official rate of exchange for such currencies, unless otherwise authorized by Congress, nor shall any such agreement relate to any subject other than the use and expenditure of such currencies or credits for currencies for the purposes herein set forth: *Provided further,* That for the purpose of selecting students and educational institutions qualified to participate in this program, and to supervise the exchange program authorized herein, the President of the United States is hereby authorized to appoint a Board of Foreign Scholarships, consisting of ten members, who shall serve without compensation, composed of representatives of cultural, educational, student and war veterans groups, and including representatives of the United States Office of Education, the United States Veterans' Administration, State educational institutions, and privately endowed educational institutions: *And Provided further,* That in the selection of American citizens for study in foreign countries under this paragraph preference shall be given to applicants who shall have served in the military or naval forces of the United States during World War I or World War II, and due consideration shall be given to applicants from all geographical areas of the United States.

In other words, surplus tractors, jeeps, LST's, etc. remaining in Australia, Siam, Holland, and other countries may make possible cultural interchanges between those countries and the United States, much as the Boxer Indemnity Fund was used to provide fellowships in American universities for many young Chinese. How much money will be available under the bill is not yet clear, although present indications are that it may total several score of millions of dollars. Neither is it clear what proportion of the funds is to be available for science; this will depend, in part, on the interest and activity of scientists themselves.

If this opportunity is well handled, its value to science, and to American world relations through science, will be enormous. Eight years of work in foreign countries, in constant contact with scientists in many fields, have made three conclusions compellingly clear to me.

The first is that no channel for international communication offers such complete freedom of movement as scientific interchange. No matter what the tongue of the scientist, his mathematical, physical, or chemical formula says the same thing the world over. The biome, the life history of the bird, the analysis of social organization of wandering monkey tribes, may be approached through similar thought processes. The genetics of corn in Minsk, Córdoba, and Iowa City follows the same laws. The scientific worker, no matter what his discipline,

finds a common bond with his co-worker on whatever side of the politician's "iron curtain." Furthermore, true internationalism, a feeling of mutual respect that transcends political limits, has existed for decades in the laboratories, libraries, and field stations. Houssay and Cannon, Shapley and Jeans, Leopold and Kashkorov, have never considered that a veto power might be necessary. Because of its international character, scientific aid is given and received freely and without thought of patronizing or being patronized; scientific aid is acceptable without question, and the giving of it is an accepted responsibility. Men have been united by science since the time of the Renaissance, and political internationalism can learn much from the scientific pattern.

However, despite the great debt of the United States to the science of the rest of the world, American scientists during the past two or three decades have shown a disturbing tendency toward parochialism. There are so many of us and we have become so content with living on our own fat that in many fields we have lost the stimulating beneficence of contact with scientists in other parts of the world. A distinguished European ornithologist once said to me: "The trouble with American mails is that they move in only one direction—outward." In part because we have been too lazy to command foreign languages, thousands of us have little knowledge of important research that is being carried on abroad; a very general ignorance of Spanish and Portuguese cuts us off from investigations in Europe, Mexico, Uruguay, Argentina, and Brazil. Even were we better prepared in the use of languages, we should still need closer contact with co-workers about the world. Were it possible for more of us to work in foreign laboratories and field stations, to hammer out our ideas on other people's anvils, to sit down face to face with our scientific fellows, and, above all, to understand the opportunities and limitations of the environment in which our colleagues are working, it would give our own science a revivifying injection of adrenalin. To know, for example, that one of the world's most productive ecologists has less than $200 a year, apart from his own small salary, for all field and laboratory expenses should give an encouraging lift to any college professor trying to maintain his research program in the face of expenses that are mounting as rapidly as GI enrollments. To learn that the total budget of the Bureau of Animal Husbandry in an eastern European country is less than $400 a year should help our thinking about the problems of Greece, Turkey, and their neighbors. We are likely to identify other parts of the earth with the United States and try to make geography fit our premises rather than our premises fit geography! In foreign countries I have often seen American technologists feeling thoroughly abused because the entire complex in which they were working was so different from Kansas or Iowa; in Korzybski's useful phrase, their maps do not fit the territory in which they must operate.

In many fields, foreign experience would widen and deepen our own research potentialities. Our zoologists and botanists need to know the tropics. "To such students," writes Harold J. Coolidge, executive secretary of the Pacific Science Board (*Science*, January 31), in a personal letter to Senator Fulbright, "the possibility of working on ecological problems in New Guinea or zoogeography where Wallace did his field work represents nothing more than a naturalist's dream, far from any hope of realization." Our museums have great gaps in their collections. Our anthropologists can enormously lengthen their horizons by work around the fringes of the Pacific. As our scientists further develop the sense of political responsibility they have begun to show, and play an increasingly influential part in the shaping of America's national and international policies (which, we are beginning to realize, are inseparable), they will be far more valuable citizens for their understanding of foreign environments—in the broad sense that includes physical as well as intellectual and other cultural factors.

Finally, the American scientist abroad is one of the world's most useful citizens. Despite our many shortcomings, we have much that many other countries need. In dozens of nations, even university curricula do not include the teaching of basic sciences. In man's struggle to survive in environments that are rarely as favorable as those of the United States, the dice are loaded against him because of the lack of scientific information. On millions of overpopulated square miles living standards are dropping, often at accelerating rates, in large part because of man's failure to understand and abide by biophysical laws. A concrete example is the complete dependence of some 80,000,000 people in Latin America on wood for cooking, heating, and many industrial purposes. Yet there is not a Latin-American country that maintains a sustained-yield forestry program; nowhere in an area twice the size of the United States, with nearly as large a population, is there such a forest products laboratory as we have at Madison, Wisconsin. Scores of millions of acres of topsoil have been lost through cut-and-get-out forest exploitation methods; hundreds of people have been drowned by floods caused primarily by deforestation; silt from deforested slopes is ruining desperately needed agricultural land in a great area where less than 10, and perhaps not over 5, per cent of the land surface is suitable for agriculture. And not more than two Latin-American countries possess good forestry schools!

Diseases killing thousands of people a year are so little understood that not even the taxonomy of their insect vectors is known. Countries whose normal nutritional level (1947) is below that of German prison camps know nothing of their climatology, soils, and hydrologic regime, or such ABC's of the land manager as plant

associations, successions, etc.; nor has their nutrition been more than approximately studied. Not only do we not have information as to what species of plants and animals are threatened with extermination, in the case of threatened species we do not know enough of their biology to set up a restoration program. Mapping, basic to so much scientific research, is retarded in most of the world; one country recently discovered, by courtesy of the AAF, that, instead of having an area of 13,000 square miles, it possesses only a little over 8,000! The mere knowledge of indicator species of plants, were it available today, would *literally* be worth tens, and quite possibly hundreds, of millions of dollars to the single nation of Venezuela, which is confronted with one of the most difficult conservation problems now in existence. I have specifically mentioned Latin America because of firsthand acquaintance with a number of its countries; similar situations obtain, however, in most other parts of the world. The vast lacunae in land-use sciences also have counterparts in many other fields.

That the support of such scientific work was the intention of the author of the Fulbright Bill is made clear by further excerpts from the letter of Mr. Coolidge, quoted above, and Senator Fulbright's reply. Mr. Coolidge writes in part:

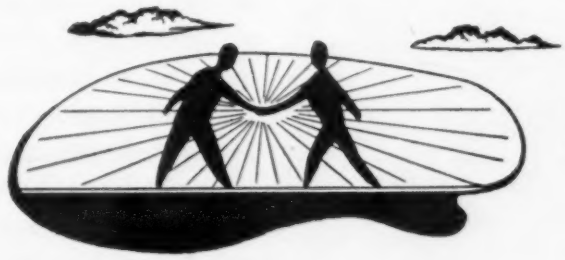
> I feel that there are two important kinds of help required to enable the qualified student to engage in field research. First, the assurance of a friendly reception and extension of certain facilities by the government of the foreign country concerned. This is a matter that can usually be arranged with the assistance of the State Department, and should not present great difficulties for Americans in most countries in the postwar world. Secondly, the highly difficult problem of finding funds to finance travel and field or laboratory research in the foreign country where the research is to be undertaken.
>
> The Fulbright Bill makes it possible through the Board of Foreign Scholarships, with the assistance of the State Department, to solve this serious problem in a way that should not only greatly benefit the student, as well as the foreign country involved, but should likewise assure the possibility of great strides in the advancement of fundamental scientific knowledge and the training of competent men, particularly in the fields of the natural and related social sciences. . . .
>
> I sincerely hope that provisions will be made to insure the participation of well-known scientists on your Board of Foreign Scholarships.

To this letter Senator Fulbright replied:

> I wish to acknowledge your very thoughtful letter of March 10. I am in accord with your views about the possibilities of the bill which I introduced.

The export of American science to other parts of the world, and the benefit to the United States through scientists participating in this export, such as would be possible under the Fulbright Bill, would probably contribute as much to a stable, peaceful world as could any human activity.

What the people of the United States get from their government depends largely on what they ask for. Despite the considerable sums we may hope for under the Fulbright Bill, these funds are, of course, limited. Many interests will be competing for them. Unless science speaks clearly, vigorously, and soon, it is not likely to participate to any considerable extent. It is to be hoped that the scientists from the United States will see the opportunity presented to them under this bill and insist, through their organizations, that science be given its full share.



A New Class of Antifilarial Compounds[1]

Arnold D. Welch, Lawrence Peters, Ernest Bueding, Arthur Valk, Jr., and Aeme Higashi

Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio

THE OCCURRENCE OF FILARIASIS IN members of the Armed Forces stationed in South Pacific areas led to organization by the National Research Council, in 1944, of coordinated investigations of the chemotherapy of this disease. The potency and the margin of safety of organometallic compounds, now used in the treatment of filariasis, may be improved by continued research; however, it was decided to concentrate the effort of this laboratory on compounds containing no heavy metal, in the hope of disclosing a new approach to the chemotherapy of this disease.

Unfortunately for chemotherapeutic research, the human form of the parasite, transmitted by various mosquito vectors, has not been found in other animal species, and it was necessary to restrict the study of new compounds to animals infested with closely related, but not identical, filarial parasites. For this purpose the most practical approach to the problem was afforded by the use of the wild cotton rat, which frequently harbors *Litomosoides carinii*, a filarial worm that resides in the pleural cavity rather than in the lymphatic system (*1*).

Although the details of the techniques employed in "screening" compounds *in vivo* for possible antifilarial activity underwent many modifications as the studies progressed, all procedures were based on the principle that each compound should be given in an amount approaching that maximally tolerated by the animal host. Further, it was considered that the frequency of dosage should be such as to favor the maintenance of a concentration of drug in the tissue fluids bathing the parasite. It was believed that these precautions might increase the possibility of detecting minimal activity in a compound, as a lead for further study.

In general, compounds were administered intraperitoneally at maximally tolerated doses every 8 hours for a total of 18 doses. Forty hours after the final injection, autopsy was performed, and the adult filariae were removed aseptically from the pleural cavities and placed in a sterile nutrient medium for observation; worms removed from an untreated rat were observed simultaneously. Characteristically, unaffected worms remained motile for at least two days, when observed at room temperature. When motility was absent and did not appear within about 8 hours after the worms were removed from the rats, the filariae were considered dead, and other criteria of death supported the validity of this simple measurement.

The effect of drug treatment on microfilariae, either *in vitro* or *in vivo*, was not studied, since it was known that the susceptibility of the embryos may differ from that of the parent worms, and it was the latter only toward which therapy was directed. Also, it was felt that "screening" of unrelated chemical substances for filaricidal activity *in vitro* would give information more likely to be misleading than helpful. Later, when a lead was obtained from studies *in vivo*, and more had been learned concerning the metabolism of these filariae, studies *in vitro* became of great importance.

Among the many compounds studied, none was found to possess appreciable activity until a member of the group of compounds known as the cyanine dyes was tested. This compound, (1-amyl-2,5-dimethyl-3-pyrrole) (1,6-dimethyl-2-quinoline) dimethinecyanine chloride (Chemotherapy Center #348), was completely curative in the maximally tolerated doses used. On further study it became evident that a very high degree of activity was present, since the intraperitoneal injection of 0.1 mg./kg. at 8-hour intervals for 18 doses regularly killed all filarial worms in all the treated animals. Fortunately for the chemotherapeutic program, the high activity of #348 was found to be shared by many others of a large group of compounds synthesized by L. G. S. Brooker and his associates, of the Eastman Kodak Company and supplied to the Committee on Medical Research of the National Research Council through Parke, Davis & Company.[2]

The cyanines were also strikingly active *in vitro*, not only in causing a rapid disappearance of motility but also in inhibiting the consumption of oxygen by adult filariae.

[1] The work described in this paper was done, in part, under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Western Reserve University (August 1, 1944–October 31, 1945); in part, under a contract between the Office of the Surgeon General, U. S. Army (November 1, 1945–December 31, 1946); and in part, with the aid of a grant from the U. S. Public Health Service (since January 1, 1947).

[2] From the beginning of the study of this group of compounds, we have enjoyed the finest cooperation from Dr. Brooker and from Parke, Davis Laboratories. Further, this investigation has been facilitated in innumerable ways by Lucille Farquhar, technical aide of the National Research Council, who coordinated studies in this and related fields. Other members of this series of compounds have been studied by R. N. Bieter, H. N. Wright, and their associates at the University of Minnesota.

The oxidative metabolism of the worms was inhibited by concentrations of ✱348 ranging from 1:25,000,000 to 1:6,000,000, and the decrease in oxygen consumption was associated with a compensatory increase in aerobic glycolysis and a decrease in glycogen synthesis. Under anaerobic conditions no effect on glycolysis was observed. Only with concentrations 1,000–2,000 times higher was the oxygen consumption of mammalian tissue slices or homogenates affected by these compounds, and such concentrations caused severe injury at the site of subcutaneous or intramuscular injection.

For the following reasons it is postulated that these drugs exert their chemotherapeutic effect through inhibiting one or more enzyme systems concerned with oxidative metabolism: (1) Worms removed from rats treated with subcurative doses of active members of the cyanine series showed markedly depressed respiratory activity and an increase in aerobic glycolysis; (2) of the large series studied, every compound active *in vivo* inhibited filarial respiration *in vitro*.

As the study of the cyanines progressed, it became evident that activity in inhibiting filarial respiration *in vitro* could be retained despite rather radical variations in structure. Almost all cyanines (and many styryl) dyes show the effect to some extent, although the activity is by no means always of a high order. The grouping characteristic of the cyanine (and styryl) dyes, whether highly or weakly active, is the amidinium-ion system in which a positively charged quaternary nitrogen is linked

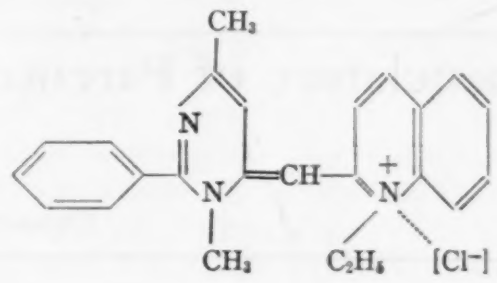
$$\rangle \overset{+}{N}{=}C{-}(C{=}C)_n{-}N\langle \leftrightarrow \rangle N{-}C{=}(C{-}C)_n{=}\overset{+}{N}\langle$$

to a tertiary nitrogen by a conjugated chain consisting of an uneven number of members. One or both of the nitrogens may be part of a heterocyclic ring, but activity is not restricted to any particular ring. Any modification which destroys the possibility of amidinium-ion resonance in the compounds causes a disappearance of high activity both *in vitro* and *in vivo*.

Variations in the manner of administration of active members of the series indicated that the drugs were effective when given intravenously, as well as intraperitoneally, but only occasional cures followed massive oral dosage. Cures followed subcutaneous administration of the drugs only when doses equal or close to those maximally tolerated by this route were used. Furthermore, subcutaneous or intramuscular injection caused damage to the tissues which, with certain members of the series, was very severe. The effectiveness of intraperitoneal administration once daily was slightly greater than that following administration every 8 hours; thus, with ✱348, a total of 1.8 mg./kg. was required when administration was at 8-hour intervals for 6 days, while a total of 1 mg./kg. was curative when the drug was given once daily for 5 days. Actually, cures could be obtained when animals were given a single dose of 1.35 mg./kg.

Since the intravenous route of administration of the drugs appeared to be the only feasible one for man, study of the activity of various members of the series was made in cotton rats, using this mode of administration. Attention was also given to the comparative damaging effects on tissues, in view of the possibility of extravasation.

One member of the series was clearly outstanding; this compound, Chemotherapy Center ✱863, is probably of the following structure, a name for which is 1′-ethyl-3,6-dimethyl-2-phenyl-4-pyrimido-2′-cyanine chloride, although an isomeric structure is possible.



In infested cotton rats, cures were almost invariably produced when ✱863 was given intravenously in doses of 1.0 mg./kg., repeated 3–6 times at intervals of 1, 3, or even 7 days. This indicates clearly, as did the earlier intraperitoneal studies with ✱348, that curative results can be correlated rather closely with the total amount of drug administered over a wide range of dosage intervals. This situation resembles that observed with certain organometallic drugs, e.g. as used in the treatment of syphilis. Toxic effects, according to the dosage schedules described, were seen only with individual doses of 10 mg. or more/kg. Accordingly, this route of administration appeared to offer a considerable margin of safety.

Extensive studies of the chronic toxicity of ✱863 in dogs and in monkeys have been based on the findings in cotton rats. These studies disclosed a mild and reversible renal damage as the only manifestation of chronic toxicity.[3] During intravenous administration there is a transient hypotensive effect, with compensatory tachycardia; this effect is of consequence only when large doses are rapidly administered.

A method for the extraction of ✱863 from tissues and its spectrophotometric determination at 494 mμ has been devised. The compound rapidly disappeared from the blood of dogs after intravenous administration, but urinary excretion rarely exceeded 5 per cent. Recovery experiments indicated that the drug is metabolically altered. The material is remarkably concentrated in the kidney; when dried from the frozen state, the drug was visible microscopically, predominantly in the convoluted tubules.[4] This finding may account for the observed renal toxicity.

[3] We are indebted to W. B. Wartman for his cooperation in the pathological examination of the tissues of animals subjected to treatment with ✱863.

[4] These observations were made by Normand L. Hoerr and Arnold Lazarow, to whom our thanks are due.

Studies of the possible effectiveness of *863 in the treatment of human patients infested with the filariae of *Wuchereria bancrofti* have been initiated through the facilities afforded us by the School of Tropical Medicine, San Juan, Puerto Rico.[5] The drug was administered to 27 patients, using various intravenous dosage regimes, without manifestations of systemic toxicity other than transient mild hypotension and tachycardia of no clinical significance. Since the drug usually does not cause an immediate disappearance of microfilariae, in either cotton rats or man, studies of the peripheral blood may be required for many months in order to determine whether sterilization or death of the parent worms has been accomplished.

[5] We are greatly indebted to the director, P. Morales-Otero, for many courtesies; to José Oliver-González, who procured the patients and gave us constant help; and to F. Hernández-Morales, D. Santiago-Stevenson, and Ramón Suárez, Jr., for their clinical aid and excellent cooperation.

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1. CULBERTSON, J. T., and ROSE, H. M. *J. Pharm. exp. Therap.*, 1944, 80, 189.

Nomenclature of Parenteral Proteases

John H. Ferguson

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RECENT INTEREST IN CERTAIN PROteases, which participate in blood coagulation (*5*, *21*) and indirectly related proteolytic phenomena, e.g. fibrinolysis (*3*, *16*, *19*), has run into a confusion of nomenclature which should be settled by general agreement. The story of the *parenteral* proteases and fibrinolytic phenomena was fully reviewed in the monumental work of Oppenheimer (*18*), whose classificatory principles have been widely accepted, with some more modern modifications.

PROTEASE, in the broadest sense, refers to all enzymes associated with protein hydrolysis. PROTEINASE is a general term appropriately used when the substrate is the whole protein molecule. Owing to multiplicity of substrates, enzymes acting under this head must be subclassified, empirically, under such generic terms as (1) *peptases*, (2) *cathepsins* (which has largely replaced the older term, ereptases), and (3) *tryptases*, for the three most common types of animal origin; and (4) *papainases*, for an important group of plant proteinases. It is distinctly intended that these terms group together enzymes on the basis of certain similarities, in the case of the first three, to the well-known alimentary prototypes, pepsin, erepsin, and trypsin(s), *disregarding* differences in origin and certain other differences, e.g. in mode of activation, inhibition, substrate specificity, stability, purity, etc. Even pH optima are currently minimized, as chiefly a matter of protein stability and purity. The recent identification of certain proteinases as crystalline proteins (*17*) and the newest means of testing on pure synthetic polypeptide substrates (*1*) are steps toward characterization of a few of these enzymes by their chemical specificity, in terms, for example, of certain linkages in the substrate molecule. The crystalline enzymes thus studied, however, show multiple points of attack on the protein (polypeptide) molecule. Hence, this approach is more successful as a basis for identification of the *individual* enzymes than as a means of classification (cf. *1*).

The Nobel-laureate work of the Rockefeller investigators (*17*), significantly extending the pioneering efforts of Willstätter and others, clearly outlines the general principle that each proteolytic enzyme really constitutes a *complex system*. This is especially well exemplified in the case of pancreatic trypsin: An inactive precursor or zymogen (TRYPSINOGEN, crystalline) is converted into active enzyme (TRYPSIN, crystalline), particularly through the mediation of an "activator," e.g. ENTEROKINASE (*17*), MOLD KINASE (*11*), etc.[1] A crystalline polypeptide (TRYPSIN INHIBITOR, *pancreatic*) inactivates fully-formed trypsin by formation of a crystalline inactive TRYPSIN + INHIBITOR compound (*17*). A recently crystallized protein TRYPSIN INHIBITOR from *soybean* (*12*) probably acts in the same way. Since there is multiplicity both of inhibitors and of the proteases they inhibit (e.g. chymotrypsin and plasma-tryptase, also), the nomenclature, ANTITRYPSIN, should be used with these reservations. The possibility of KINASE inhibitors, directed against the "activators" rather than against the protease proper, is not fully explored in the work on the pancreatic enzymes.

The "thromboplastic-enzyme" theory of blood coagulation (*5*) draws attention to similarities between the experimental actions of pancreatic trypsin and natural TRYPTASE enzymes demonstrable in, but not yet isolated from, plasma (serum), blood corpuscles (including platelets), and tissue source materials. Very recent work (*6*) is completely confirmatory of this idea and suggests adoption of the following nomenclature, in close analogy with the pancreatic tryptase system:

I. TRYPTASE: active protease, prefixed by name of

[1] Crystalline trypsin assists its own formation from crystalline trypsinogen in an autocatalytic manner, and certain factors, e.g. CALCIUM, are important accessories because they prevent loss of enzyme through side reactions of an inactivating nature (*14*).

source material, e.g. *serum*-tryptase, *brain tissue*-tryptase, etc.

II. TRYPTOGEN: inactive precursor on the enzyme, similarly prefixed.

III. TRYPTOKINASE: general term for "activators" of tryptogen, including *streptococcal* TRYPTOKINASE or STREPTOKINASE ("streptococcal fibrinolysin" is criticized below) and suspected *physiological* tryptokinase factor(s) (*9*).

IV. ANTITRYPTASES: tryptase inhibitors (see above), including proved (*6*) actions of the (crystalline) trypsin inhibitors of *pancreatic* (*17*), *soybean* (*12*), and *egg-white* (*6*) origin, *serum*-antitryptase (as yet unidentified), etc. (*10*).

V. ANTITRYPTOKINASES: inhibiting the tryptokinase "activator," including the clearly demonstrated antibody detected in blood after streptococcal infections ("streptococcal antifibrinolysin,"*10*).

TRYPTASE merely means trypsin-*like*, in many experimental situations (*5*). Other suggested terms are criticized as follows: The time-honored term, "FIBRINOLYSIN" (*3, 16, 19*), most recently revived by Loomis, *et al.* (*13*), must be discarded because (1) it suggests a specificity for *fibrin* substrate which is quite unfounded according to data going back to the earliest investigations; and (2) much confusion carries over from the erstwhile failure to distinguish enzyme and its activator(s), e.g. "streptococcal *fibrinolysin*"(*8*) (now recognized as a misnomer, *2*). "FIBRINOLYTIC PROTEASE," as a descriptive noncommittal term, is acceptable (*10*). "PLASMIN" is the latest suggestion (*2*) but is objectionable because (1) it indicates a *plasma* origin and ignores similar protease(s) from tissue (cellular) sources; (2) the plasma presumably gets it from some cellular source in the first place; (3) pending isolation and identification, a specific name is premature; (4) Christensen dismisses, perhaps too lightly, the all-but-forgotten use of the term (Fr. *plasmine*) for a crude salt-precipitated mixture of plasma proteins, by Denis (*4*), which retains historical interest both in connection with coagulation (fibrinogen) and as the first step toward the modern general method of isolation of proteins by fractional precipitation.

TRYPTOGEN (*5*) is preferred to "PLASMINOGEN" for the same reasons. Names like "LYTIC FACTOR" (*15*) are merely preliminary to the establishment of the definite idea. "PROFIBRINOLYSIN" (*13*) must be ruled out because "FIBRINOLYSIN" is inacceptable.

STREPTOKINASE (*2*) is quite acceptable for the streptococcal "activator," especially when it is recognized as one member of a group (hence, *streptococcal*-TRYPTOKINASE) which merits the general term, TRYPTOKINASE.

ANTITRYPTASE(S), again, is a good group name, conveniently used in lieu of TRYPTASE INHIBITOR, and the inclusion of known ANTITRYPSINS (TRYPSIN INHIBITORS) is as interesting as a priori considerations would lead us to anticipate. "ANTIFIBRINOLYSIN" (*13*), following long usage (cf. fibrinolysin), would mean antienzyme, but suffers in light of the criticisms against calling the protease by this term. The use of "ANTIFIBRINOLYSIN" (*10*) for the immunological inhibitor of the *kinase* obviously causes confusion. "ANTIPROFIBRINOLYSIN" is not much better, since it is also involved in the ambiguity of "fibrinolysin." ANTITRYPTOKINASE, therefore, is logically preferred, with ANTISTREPTOKINASE admissible as a special case. Notwithstanding noteworthy differences in origin (*22*), kinase activators (*10*), and exact modes of proteolytic action (*2, 7*), the very striking similarities of natural plasma tryptase to pancreatic trypsin in general proteolytic effects and, particularly, in relation to blood clotting, fully justify the suggested group nomenclature. This classificatory terminology, moreover, has permanent value, even when the individual members of the class become separately characterized on the basis of biochemical character and substrate specificities.

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It is proposed to hold an informal meeting at the Stevens Hotel, Chicago, on the evening of Sunday, May 18, on the occasion of the annual meetings of the Federation of American Biological Sciences, at which this topic may be discussed by interested workers. The author would welcome the names of those who wish to attend and the comments of others, unable to be present, who would like their views to be presented at this meeting.

The present publication is part of a project on "Enzymes and enzyme inhibitors in relation to blood coagulation and hemorrhagic disorders," aided by a grant from the John and Mary R. Markle Foundation.

Obituary

William Perry Hay

1871–1947

William Perry Hay, naturalist and educator, died at his home in Bradenton, Florida, on January 26, 1947, at the age of 76. He was born at Eureka, Illinois, on December 8, 1871; was graduated from Butler University, Indianapolis, in 1891; began his teaching as head of the Department of Biology in the Washington, D. C., high schools in 1892; and taught in a number of schools and colleges in and about Washington until the time of his retirement in 1934.

He grew up in a home of biological tradition, his father, Oliver P. Hay, of the U. S. National Museum, being one of the foremost students of both living and fossil reptiles. The son, though mainly busied with teaching, was also a herpetologist in his own right. Retirement brought him leisure, which he employed to the end of his working days in the study of his favorite groups, the snakes and salamanders. He had prepared the many detailed and accurate drawings needed for a comprehensive work on North American herpetology and had almost completed the text at the time of his death.

Before retirement from teaching Prof. Hay lived at Kensington, Maryland, and was an active participant in the work of a number of Washington scientific societies. He was a founder of the Washington Biologists' Field Club, and when that club was incorporated in 1901, he was elected president. He was a chief promoter of one of the Club's most unique and important enterprises: the establishment of field headquarters and the erection of a building for it on Plummer's Island in the Potomac River. This bit of earth has since become, with respect to its resident fauna and flora, one of the best-known spots in the whole world.

During World War II he had a large share in directing the useful service of the Hegener Research Supply of Sarasota. When the chief medical laboratories of the Nation were calling for the tropical animals needed in their research work, Prof. Hay offered his zoological knowledge and practical laboratory experience in order to aid in supplying the necessary animals. For this work he was awarded a Certificate of Merit by the Office of Scientific Research and Development, on recommendation of its Committee on Medical Research.

Twice in his time Prof. Hay accumulated a considerble zoological library. On retirement from teaching he gave the greater part of his books to the library of the U. S. National Museum. While in Florida he again gathered together books of great value for the use of college students, and these he gave to the Department of Zoology of the University of Florida, Gainesville. He was ever a friend of youth.

JAMES G. NEEDHAM

Lake Placid, Florida

Harris Perley Gould

1871–1946

Harris Perley Gould, former head of the Division of Fruit and Vegetable Crops and Diseases, Bureau of Plant Industry, Soils and Agricultural Engineering, U.S. Department of Agriculture, died October 17, 1946, in Washington, D. C.

Mr. Gould was born at North Bridgton, Maine, September 6, 1871, the son of Charles Henry and Bertha S. (Wadsworth) Gould. He was graduated from the University of Maine with the B.S. degree in 1893 and received the M.S.A. degree at Cornell University in 1897. From 1899 to 1901 he served as assistant entomologist and horticulturist at the Maryland Agricultural Experiment Station. His early horticultural research resulted in several publications at each of these institutions.

Upon organization of the Bureau of Plant Industry in 1901 Mr. Gould joined the staff as assistant pomologist and was actively engaged in horticultural research and administration until his retirement in 1941, after three years as head of the division that includes all Federal horticultural investigations. He was an outstanding authority on fruit varieties and conducted extensive regional studies on their adaptation to climatic and physiographic conditions, particularly in southern and eastern fruit-growing sections. The results of his studies are included in 15 Farmers' Bulletins and some 25 technical and popular articles on horticultural subjects. He was also the author of a book entitled *Peach growing*, in the Rural Science Series. As collaborator, he continued his active interest in pomology after his retirement. The habits of industry acquired on a New England farm became a part of his character. To all horticulturists, professional and practical, he gave generously of his time and effort, and his interest in them and in the science and art of fruit production was untiring.

GEORGE M. DARROW

Plant Industry Station,
U. S. Department of Agriculture, Beltsville, Maryland

NEWS *and Notes*

Brookhaven National Laboratory, now under construction on the 6,000-acre site of Camp Upton, Long Island, New York, is a government-owned, government-financed atomic research project operated by Associated Universities, Inc., under contract with the U. S. Atomic Energy Commission. The Laboratory's program will be oriented toward the development of fundamental scientific information on the nature and properties of atomic energy, its application to chemistry, physics, medicine, and biology, and improved techniques for the production of atomic power and the preparation of radioactive isotopes.

Results of studies carried on will be unclassified.

Facilities will include a graphite uranium pile, a "hot" laboratory for the purpose of separating radioactive isotopes, still another pile with 100 times the neutron flux of the first, a 30,000,000- to 40,000,000-electron volt cyclotron, a 600,000,000- to 1,000,000,000-electron volt synchrocyclotron, an electronuclear machine in which electrons or positive particles may be accelerated to energies of 1,000,000,000 volts, and various other forms of apparatus beyond the reach of individual institutions. Prior to completion of the larger equipment the staff will experiment with cosmic rays and induce radioactive substances such as C^{14}.

Ultimately, a permanent staff of 300 scientists will be assigned to the Laboratory. In addition, there will be a visiting staff of about 200 and administrative, technical, maintenance, and service personnel totaling about 2,000. It is expected that about 100 scientists will have been assigned by the fall of 1947.

Associated Universities, Inc., is a nonprofit corporation formed by 9 major eastern universities, each of which nominates two trustees. The universities and their representatives follow: Columbia University—I. I. Rabi and George B. Pegram; Cornell University—F. A. Long and A. S. Adams; Harvard University—G. B. Kistiakowsky and Edward Reynolds; Johns Hopkins University—R. D. Fowler and P. S. Macaulay; Massachusetts Institute of Technology—J. R. Zacharias and J. R. Killian, Jr.; University of Pennsylvania—L. N. Ridenour and W. H. DuBarry; Princeton University—H. D. Smyth and G. A. Brakeley; University of Rochester—George B. Collins and R. L. Thompson; Yale University—W. W. Watson and E. W. Sinnott; Between full meetings of the Board of Trustees an Executive Committee (see cover) acts with authority in determination of Laboratory policies. Eldon C. Shoup, full-time executive vice-president of AUI, is responsible for executing the policies and programs of the Board. The director of the Laboratory, Philip M. Morse, is assisted by a Scientific Advisory Committee, the membership of which is composed of the 9 scientists on the Board of Trustees. Assistant director of the Laboratory is Robert A. Patterson.

The activities of the Laboratory are to be organized departmentally around fundamental fields of research. The Physics Department, which has already begun its work, is headed by N. F. Ramsey. Also under way are the Electronuclear Machines Project, under M. Stanley Livingston, and the First Pile Project, headed by Lyle B. Borst.

In the words of the director, "By our research in physics and chemistry, we hope to learn more about the behavior of atoms so as to control atomic energy for beneficial uses. In biology and medicine, we will learn more about living organisms, in order to develop methods of treatment for diseases such as cancer and many other ills. By fundamental research in engineering, we hope to be able to speed the development of atomic power production."

The Executive Committee of the Inter-Society Committee for a National Science Foundation has endorsed S. 526 (the Smith Bill) with two suggested amendments. First is that the number of members of the Foundation be reduced from 24 to 9. Second is the recommendation that the Director be appointed by the President, after consulting with the members of the Foundation, by and with the advice and consent of the Senate. These recommendations were made on May 1 in letters to Senator Taft, chairman of the Senate Committee on Labor and Public Welfare, Senator Smith, principal author of the bill, and Representative Wolverton, chairman of the House of Representatives Committee on Interstate and Foreign Commerce. That Committee is considering science foundation bills in the House of Representatives.

The Executive Committee met in Washington, D. C., April 28. The meeting was attended by Edmund E. Day, Ralph W. Gerard, Harlow Shapley, C. G. Suits, Homer W. Smith, Douglas Whitaker, and Dael Wolfle.

About People

Carl C. Lindegren, research professor of botany, Washington University, St. Louis, spent the month of April at the University of Washington, Seattle, as a Walker Ames professor of botany. His series of lectures will be published in the near future under the title *Yeast genetics*.

Fernandus Payne, dean of the Graduate School, Indiana University, addressed the Sigma Xi Club of the University of Louisville April 18 on "The Cytology of the Pituitary Gland of the Fowl."

Peter R. Morrison, Department of Physical Chemistry, Harvard Medical School, has been appointed assistant professor of zoology and physiology at the University of Wisconsin, beginning in September.

Theodore L. Swenson, special assistant to the chief of the Bureau of Agricultural and Industrial Chemistry, Department of Agriculture, has been appointed head of the food technology

section of the Stanford Research Institute, where he will coordinate scientific research with developments in the food-processing industry.

H. H. Mottern, food research chemist, has been appointed director of research of the H. J. Heinz Company, where he has been a member of the research staff since 1945. Previously Dr. Mottern was with the U. S. Department of Agriculture.

Donald F. Jones, geneticist at the Connecticut Agricultural Experiment Station, will address the members of the Plant Institute, Ohio State University, May 19, on "Our Concepts of Hybrid Vigor Today and Yesterday." At a dinner to be held in his honor, Dr. Jones will speak on "The Development of Hybrid Seed Corn in the United States."

John A. C. Bowles, associate director, Research and Control Department, Rexall Drug Company, has been appointed director of the newly-created Product Development Laboratory, Medical Research Division, Sharp & Dohme, Inc.

Grants and Awards

Selman A. Waksman will receive the 1947 Passano Foundation Award of $5,000 at a presentation dinner scheduled for June 12, during the week of the meetings of the American Medical Association in Atlantic City. In addition to Dr. Waksman's address, "Antibiotics and Tuberculosis—A Microbiological Approach," the program will include a brief address by Sir Howard Florey, Oxford, England, who was knighted for his development of the clinical applications of penicillin.

Dr. Waksman receives the award for his original research in the field of antibiotics culminating with his discovery of streptomycin. The Passano Foundation, established in 1943 by The Williams & Wilkins Company, medical publishers, Baltimore, Maryland, provides the award to encourage medical research, especially that which has clinical application.

Clyde E. Keeler, a member of the faculty, Georgia State College for Women, Milledgeville, received the prize offered for the first time by the Association of Southeastern Biologists for the best research paper presented at its annual meeting. Dr. Keeler's prize-winning report was entitled: "Modification of Brain and Endocrine Glands as an Explanation of Altered Behavior Trends in Coat-Character Mutant Strains of the Norway Rat."

The 1947 Edward L. Bernays Atomic Energy Award of a $1,000 U. S. Government bond will be made by the Society for the Psychological Study of Social Issues to the individual or group contributing the best action-related research in the field of the social implications of atomic energy, according to an announcement by David Krech, chairman of the Award Committee. All research published or completed in 1947 or manuscripts reporting such research but not yet published are eligible for consideration. Reports must be submitted in duplicate not later than November 1, 1947. All communications relative to the Award should be addressed to Dr. David Krech, Swarthmore College, Swarthmore, Pennsylvania.

Colleges and Universities

Stanford University has announced the following promotions: Hubert S. Loring and Richard A. Ogg, Jr., professors of chemistry; Orson Cutler Shepard, professor of mineral sciencesr Reed Clark Rollins, associate professos of biological sciences; Robert Lewi; Bacon and William A. Bonner, assistant professors of anatomy and chemistry.

California Institute of Technology has adopted a new faculty salary plan based upon 12- rather than 9-month appointments, according to an announcement by Lee A. DuBridge, president. The plan will provide for a month's vacation and leave of absence either with or without pay, depending upon the type of work to be done by faculty members during such periods. The new appointment plan will enable faculty members to do research, study, preparation of course material, teaching, student supervision, and administration work on or off campus during the summer months. This plan, which will also include substantial salary increases, will become effective July 1.

Simmons College, Boston, has announced the following promotions, to become effective July 1: Philip M. Richardson, to professor of biology; Julian L. Solinger, to associate professor of biology; and Shirley T. Northrup, to assistant professor of chemistry. New appointments to the faculty are: Mary P. Crumley, instructor in biology, and Yorick G. Hurd, instructor in physics.

Elections

The National Academy of Sciences elected the following officers during its annual meeting, held in Washington, D. C., April 28–30: Alfred N. Richards, University of Pennsylvania, president for a four-year term; F. E. Wright, Carnegie Institution of Washington, re-elected home secretary for a four-year term; W. Albert Noyes, University of Rochester, and Donald D. Van Slyke, Hospital of the Rockefeller Institute for Medical Research, members of the Council of the Academy for three-year terms.

Newly elected members of the Academy are: Luis W. Alvarez, professor of physics, University of California, Berkeley; Robert F. Bacher, U. S. Atomic Energy Commission, Washington, D. C.; Paul D. Bartlett, professor of chemistry, Harvard University; Jacob Bjerknes, professor of physics, University of California at Los Angeles; Francis G. Blake, dean of Yale University School of Medicine; R. Alexander Brink, chairman, Department of Genetics, University of Wisconsin; Ralph W. Chaney, professor of paleobotany and curator of paleobotany, Museum of Paleobotany, University of California, Berkeley; Arthur C. Cope, professor in charge of Department of Chemistry, Massachusetts Institute of Technology; Farrington Daniels, professor of physical chemistry, University of Wisconsin; Arnold Gesell, director, Clinic of Child Development, Yale University School of Medicine; James Gilluly, professor of geology, University of California at Los Angeles; R. B. Goldschmidt, professor of zoology, University of California, Berkeley; Samuel A Goudsmit, professor of physics, Northwestern University; C. H. Herty, Jr., research engineer and assistant to vice-president, Bethlehem Steel Company; Frederick L. Hisaw, professor of zoology, Harvard University; Wolfgang Köhler, professor of psychology, Swarthmore College; L. G. Longsworth, associate member, Rockefeller Institute for Medical Research; Edwin M. McMillan, professor of physics, University of California, Berkeley; Walter J. Meek, acting dean, Medical School, University of Wisconin; J. L. Oncley, director, Ultracentrifuge Laboratory, Harvard University Medical

School; Lars Onsager, professor of chemistry, Yale University; John P. Peters, professor of medicine, Yale University; Paul A. Smith, professor of mathematics, Columbia University; C. Richard Soderberg, professor of applied mechanics, Massachusetts Institute of Technology; Paul Weiss, professor of zoology, University of Chicago; F. W. Went, professor of plant pathology, California Institute of Technology; Robert E. Wilson, chairman, Board of Directors, Standard Oil Company of Indiana; and E. Bright Wilson, Jr., professor of chemistry, Harvard University.

New foreign associates of the Academy are: P. A. Alexandroff, professor of mathmatics, University of Moscow; K. Linderstrøm-Lang, head, Chemical Division, Carlsberg Laboratory, Copenhagen, Denmark; J. N. Bronsted, professor and director, Institute for Physical Chemistry, Copenhagen, Denmark; Björn Helland-Hansen, director, Geophysical Institute, Bergen, Norway; and Frederic Charles Bartlett, director, Psychological Laboratory, Cambridge, England.

Walter D. Lambert, U. S. Coast and Geodetic Survey, president of the International Association of Geodesy, on January 13 was elected a correspondent of the Paris Academy of Sciences, Institut de France, in the Section of Geography and Navigation. He succeeds Father Pierre Lejay, who was elected a nonresident member of the Academy.

Wendell G. Scott, associate professor of clinical radiology at Washington University School of Medicine, has been re-elected president of the St. Louis Radiological Society for 1947.

The Hawaii Chapter of the Society of the Sigma Xi was officially installed March 19 in Honolulu during the University of Hawaii's 40th anniversary celebrations. Harlow Shapley and Karl T. Compton installed the following officers: John H. Beaumont, director of the University of Hawaii Agricultural Experiment Station, president; Robert W. Hiatt, associate professor of zoology, vice-president; O. A. Bushnell, assistant professor of bacteriology, secretary-treasurer; and Janet Smith, associate professor of education, and C. E. Pemberton, chief entomologist, Hawaiian Sugar Planters' Association, councilors.

The Hawaii Chapter is the 98th chapter to be formed and the first to be recognized by the national society beyond the continental limits of North America.

The Eastern Psychological Association elected the following officers at its meeting in Atlantic City on April 25–26: J. McV. Hunt, Institute of Welfare Research, Community Service Society of New York, president, 1947–48; Harold Seashore, Test Division, Psychological Corporation, secretary, 1947–49; Weston A. Bousfield, University of Connecticut, treasurer, 1947–50; O. Hobart Mowrer, Graduate School of Education, Harvard University, and Helen Peak, Connecticut College for Women, directors, 1947–50.

Recent Deaths

Morgan Brooks, 86, professor emeritus of electrical engineering at the University of Illinois, died April 23 in Washington, D. C.

Sir Almroth Wright, 85, fellow of the Royal Society and former director of the Institute of Pathology, St. Mary's Hospital, London, died at his home, Farnham Common, Buckinghamshire, on April 30. Sir Almroth originated the system of inoculations for typhoid, enteric tuberculosis, and pneumonia and developed methods to measure their effects on the blood.

Abel Joel Grout, 80, bryologist and author of many books on mosses, died March 27 in East Bradenton, Florida.

The 50th annual volume of *The Bryologist,* journal of the Sullivant Moss Society, will be dedicated to Dr. Grout, founder of the journal and co-founder of the Society, according to an announcement by the editor, W. C. Steere, Department of Botany, University of Michigan. It is expected that the special anniversary issue will contain more than twice its usual number of pages.

J. Hunter Gooding, Jr., 55, sales manager of the Semesan Division, Grasselli Chemicals Department, Du Pont Company, died April 14 after an illness of more than a year.

Discovery of an Upper Pleistocene Human Skeleton at Tepexpan, Valley of Mexico

The studies on Early Man in the Valley of Mexico which have been carried out by the writer since November 1945 with the aid of the Viking Fund, Inc., of New York, and with the cooperation of the Instituto Nacional de Geologia and the Instituto de Antropologia e Historia in Mexico City, reached a successful climax on February 22 with the discovery of a fossil human skeleton in the Upper Pleistocene Becerra formation near the village of Tepexpan, in the State of Mexico. The well-fossilized bones were found in an excavation at a depth of 1.12 meter in a buff-colored, silty clay—the same layer which had previously yielded several skeletons of the imperial elephant.

The geologic position and preservation of this fossil is such as to exclude all possibilities of intrusive burial or redeposition. It was found 30 cm. deep below the caliche formation, which in this region marks the beginning of the early Recent period. The caliche was diagnosed first by Prof. Kirk Bryan, of Harvard University, as a dry-climate fossil soil which represents the same dry climatic phase recognized by Dr. E. Antevs in the American Southwest and dated by him as 10,000 years old. The preceding Becerra formation represents the last Pluvial, when the Valley of Mexico was occupied by a lake whose beaches are preserved near the site. The fossil-bearing layer marks the closing phase of the Becerra Pluvial, when the lake level had fallen and a swampy lagoon had formed near Tepexpan. It is presumed that an entire herd of mammoth was trapped on the swampy ground and that prehistoric man was somehow involved in the event.

The precise location of the excavation was given by a preliminary geophysical survey carried out by Dr. Hans Lundberg, of Toronto, Canada. The spot marked the point of greatest electrical resistance offered to an alternating current artificially introduced into the ground in the manner of the linear electrode method. Without this geophysical survey the fossil could not have been located, since the ground offered no clues other than the presence of several buried mammoth remains found scattered over a portion of a flat lake plain 3,000,000 square meters in extent. To my knowledge, this is the first successful application of a geophysical device in the search for Early Man. The total cost of the instruments did not exceed $600. The plotting of equipotential lines between two electrodes took 9 days, but might have been done more quickly had various demonstrations not interrupted Dr. Lundberg's survey.

The position of the skeleton suggests that the person, an adult male, met with an accidental death. The body lay doubled up with legs drawn up to the chest, face downward, and must have sunk partially into mud so that the buried portion escaped the scavanging action of animals which may be held responsible for carrying off the feet, hip bones, most of the chest, backbones, and shoulder blades. Such an explanation would account best for the peculiar preservation and position of the buried skeletal remains.

In this connection it is of interest to note that the writer had previously found stone and bone artifacts at three different localities in the Becerra formation. These were found in deposits containing rolled bones of elephant, bison, horse, and *Glyptodon*. Equally interesting is the fact that a small flake of obsidian was found by Ing. A. R. V. Arellano with an elephant skull some 1,000 feet distant from the new site. A fragmentary, Folsom-like point was found on the hillside near by. The artifacts from the Becerra formation include three gravers, a scraper, and a bone point.

The fossil human remains are now in the Museo Nacional de Antropologia, Mexico City. Dr. J. Romero and Miss Johanna Faulhaber cleaned the remains of the clay matrix, and Dr. Romero has given me a tentative identification. While the facial portion of the skull and the lower mandible are broken, complete reconstruction appears possible. Besides the skull there are the following, partly fragmentary bones: 2 femurs, 2 kneecaps, 2 broken tibiae, 2 fibulae, 2 collar bones, 3 small rib fragments, 1 atlas and 3 fragmentary cervicals, 2 humeri, 1 complete right radius and 1 fragmentary left radius, 2 broken ulnae, 7 wrist bones of both hands, 5 metacarpals of both hands, and 13 finger bones.

A preliminary measurement of the skull showed it to be of mesocephalic type. It is peculiarly high but does not bear any truly primitive features.

The excavation site and vicinity have been mapped by Mr. Kenneth Segerstrom, topographical engineer of the U. S. Geological Survey, on a scale of 1:5,000. The site was visited during the first week after its discovery by Dr. Clarence Ross and Mr. C. Fries of the U. S. Geological Survey, Drs. Gordon F. Eckholm of the American Museum of Natural History, Henry Field, Alfonso Caso, Eduardo Noguerra, Dr. de la Borbolla, and Ing. R. Manges Lopez, director of the Instituto Nacional de Geologia. (HELMUT DE TERRA, *Calle Tigris, Mexico, D. F.*)

Since the receipt of Dr. de Terra's note on the Tepexpan discovery Dr. Franz Weidenreich has made a preliminary report on the anatomical character of this skeleton. His report follows:

The general character of the bones indicates that the individual belongs to the recent human type (*Homo sapiens*).

Although the skull does not reveal any special primitive feature characteristic of early hominids (the total calvarial height being about 140 mm.—rather noteworthy considering the size of the skull), there are some structural peculiarities which are more primitive than those usually found in modern human skulls. The frontal and occipital superstructures are well developed. Both come very close to real torus formations. The frontal superstructure consists of a distinct eyebrow ridge on both sides. The ridge extends to the glabella region and turns downward to the frontonasal suture, forming a well-marked supranasal torus such as occurs in the Australian bushman of today and in other "primitive races." The supraorbital ridges proper show an advanced stage of deterioration, but the original character of the ridge is easily recognizable. The occipital bone exhibits a typical occipital torus which resembles even the condition found in Neanderthal skulls. Similar primitive features are recognizable at the nuchal peanum, the mastoid, and the parietal region (temporal line).

These primitive features are not restricted to the brain case. They occur also in the extremity bones in which they appear under the form of pronounced muscular tuberosities (deltoid tuberosity of the humerus, crista interossea, and crista musculi pronator quadratus of the radius).

The facial skeleton does not show any special primitive features. There is neither a general nor an alveolar prognathism. The teeth, so far as they are preserved, are those of modern man.

Regarding special racial characteristics, the present condition of the facial parts does not permit a definite diagnosis. The nasal bones are "pinched," a peculiarity frequently encountered in certain Mongoloid types (Eskimo). The cheekbone, on the other hand, is small and does not project to a marked extent neither forward or sideward. The crown of the upper incisors are not preserved; hence, it is impossible to recognize whether or not these teeth were shovel-shaped (Mongolian characteristic).

The brain case has a particular form; the vertex region is pronouncedly domed without showing any indication of artificial deformation. This shape may help to determine the special group to which the skull must be attributed.

None of the bones is very robust; on the contrary, they rather appear to be of a generally fine structure. Although this suggests female sex, the strongly developed muscular tuberosities prove that the individual was a male.

The tentative estimation of the cranial capacity is from 1,350 to 1,450 cc.

Taking all morphological facts into consideration, as far as it is possible to do so at this moment, it can be stated that none of them contradicts the possibility that the Tepexpan skeleton is that of an individual who lived at the end of the Pleistocene period. All the skeletons of Upper Paleolithic man known from Europe, Asia, and Africa already show the features characteristic of recent mankind. In most cases really primitive characteristics are completely missing. Wherever features were found recalling primitive conditions, they showed a more or less pronounced degree of deterioration, as is the case with the Tepexpan man.

Because of the inconclusiveness of the anatomical character of the skeleton, its identification as one of Pleistocene age cannot be based on anatomical evidence alone. An important criterion in this respect is the degree of fossilization of the bones. All the bones of the Tepexpan skeleton are mineralized, but the degree of mineralization varies: the lower jaw, for example, shows a higher degree than the brain case and the remaining facial bones. In the extremity bones, the mineralization led to a complete metamorphosis of the internal structure of the compacta, such as is typical of human bones from the Middle Pleistocene of China and Java.

If the stratigraphy of the Tepexpan skeleton proves the Pleistocene age, the anatomical character and the degree of its mineralization lends strong support to this assumption.

Meetings of Affiliated and Associated Societies

The following list of meetings is based on reports submitted to AAAS headquarters by society secretaries:

Section A: Mathematical Association of America, September 1–2, New Haven, Connecticut; Institute of Mathematical Statistics, December 26–31, Chicago, Illinois; American Mathematical Society, December 29–31, University of Georgia, Athens.

Section B: American Association of Physics Teachers, June 18–21, University of Minnesota, Minneapolis, and December 26–31, Chicago; American Society for X-Ray and Electron Diffraction, June 23–25, Montreal, Canada; Society of Rheology, October 30–31, New York City; American Physical Society, December 26–31, Chicago; Sigma Pi Sigma, December 26–31, Chicago.

Section C: American Association of Cereal Chemists, May 19–23, Kansas City, Missouri; American Oil Chemists' Society, May 20–22, New Orleans, Louisiana; American Chemical Society, September 15–19, New York City; American Institute of Chemical Engineers, November 9–11, Detroit, Michigan.

Section D: The Meteoritical Society, June 16–21, San Diego, California; American Astronomical Society, September, Evanston, Illinois.

Section E: American Society for Professional Geographers, December 27–30, Charlottesville, Virginia; Association of American Geographers, December 29–31, Charlottesville; Geological Society of America, December 29–31, Ottawa, Canada; Paleontological Society, December 28–31, Ottawa; National Council of Geography Teachers, December 27–29, Charlottesville.

Sections F and FG: Federation of American Societies for Experimental Biology, May 18–22, Chicago; Western Society of Naturalists, June, San Diego; Herpetologists League, June 16–21, San Diego; American Society of Mammalogists, August 24–27, Higgins Lake, Michigan; American Malacological Union, American Microscopical Society, American Society of Naturalists, American Society of Parasitologists, Ecological Society of America, Entomological Society of America, Genetics Society of America, Linological Society of America, National Association of Biology Teachers, Phi Sigma Society, and Union of American Biological Societies, December 26–31, Chicago; Beta Beta Beta, December 27–28, Chicago; American Society of Zoologists, December 29–31, Chicago.

Section G: American Fern Society, American Society of Plant Physiologists, American Society of Plant Taxonomists, Botanical Society of America, Inc., Mycological Society of America, and Sullivant Moss Society, December 26–31, Chicago; American Phytopathological Society, December 28–30, Chicago.

Section H: American Folk-Lore Society, December, Detroit, Michigan; American Anthropological Association, December 27–30, Toronto, Canada; Archaeological Institute of America, December 29–31, New Haven, Connecticut.

Section I: American Psychological Association, September 9–13, Detroit; Society for Research in Child Development, December 27, Chicago.

Section K: Population Association of America, May 17–18, Princeton, New Jersey; Econometric Society, September, Washington, D. C., and December 26–31, Chicago; Academy of World Economics, December 26–31, Chicago; American Sociological Society, December 28–30, New York City; American Statistical Association, December 26–31, Chicago; Pi Gamma Mu, December 26–31, Chicago; American Economic Association, December 27–30, Chicago; Metric Association, Inc., December 27, Washington, D. C.

Section L: History of Science Society, December, Cleveland, Ohio; Philosophy of Science Association, December 26–31, Chicago; American Philosophical Association, December 28–31, New York City.

Section M: American Society of Heating and Ventilating Engineers, June 1–4, Coronado, California; American Society of Refrigerating Engineers, June 9–11, Los Angeles, California; American Institute of Electrical Engineers. June 9–13, Montreal, Canada; American Society of Mechanical Engineers, June 16–19, Chicago; Society for the Promotion of Engineering Education, June 19–21, Minneapolis, Minnesota; American Society of Agricultural Engineers, June 22–25, Philadelphia, Pennsylvania; Illuminating Engineering Society, September 15–19, New Orleans, Louisiana.

Section N: Society of American Bacteriologists, May 13–16, Philadelphia; American Society of Experimental Pathology, May 17–22, Chicago; American Physiological Society, May 18–22, Chicago; American Psychiatric Association, May 19–23, New York City; American Medical Association, June 9–13, Atlantic City, New Jersey; American Association of Dental Schools, June 23–25, Chicago; American Association of Colleges of Pharmacy, August, Milwaukee, Wisconsin; American Veterinary Medical Association, August 18–21, Cincinnati, Ohio; American Pharmaceutical Association, August 24, Milwaukee; American Roentgen Ray Society, September 14–19, Atlantic City; American Public Health Association, October 6–10, Atlantic City; American Academy of Ophthalmology and Otolaryngology, October 12–17, Chicago; American Dietetic Association, December 26–31, Chicago.

Section O: Association of Official Seed Analysts, June 2–5, Richmond, Virginia; Agricultural Institute of Canada, June 23–26, Lethbridge, Alberta; American Dairy Science Association, June 24-26, Ontario, Canada; American Society of Animal Production, November 28–29, Chicago; Society of American Foresters, December 18–20, Minneapolis; American Society for Horticultural Science, December 26–31, Chicago; Potato Association of America, December 27–29, Chicago.

Section Q: Pi Lambda Theta, August 10–13, Portland, Oregon; Canadian Teachers' Federation, August 11–15, Halifax, N. S.; National Science Teachers Association, December 26–31, Chicago; Phi Delta Kappa, December 27–31, Kansas City, Missouri.

All Sections: Research Council on Problems of Alcohol, May, New York City, and December 26–31, Chicago; American Nature Study Society, Sigma Delta Epsilon Graduate Women's Scientific Fraternity, and Society of the Sigma Xi, December 26–31, Chicago.

TECHNICAL PAPERS

Chemotherapeutic Investigations of Cyanine Dyes

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Although extensive investigations have been carried out on the chemotherapeutic properties of the cyanine, styryl, and related dyes by Prof. Browning and his collaborators at the University of Glasgow (*1*), the chief use of these dyes has remained in the field of photography, where they are indispensable as color sensitizers. Because of their significance in this connection, a very large number of new dyes of these classes has been prepared during the past 20 years in the Research Laboratories of the Eastman Kodak Company, in the department of one of us (L. B.) who, prompted by the earlier work of Browning, was eager to see the pharmacological investigations extended and the newer cyanine dye types in particular given adequate chemotherapeutic testing. An arrangement was reached whereby certain representative compounds were prepared[1] in a suitably soluble form and submitted for extensive testing.

Some of the dyes were supplied to the National Research Council Chemotherapy Center for Tropical Diseases for testing against the organisms of such diseases. The most striking fact to emerge from the investigations which ensued was the pronounced antifilarial and anthelmintic activities of many of the cyanine types.[2] Many of the dyes also showed antimalarial activity, but not such as to equal that of drugs already available. The antimalarial results have been reported (*2*).

Another extremely interesting activity was noted in our laboratories when (1-amyl-2,5-dimethyl-3-pyrrole) (1,6-dimethyl-2-quinoline) dimethinecyanine chloride was tested *in vitro* against the lactic acid-producing bacilli.[3] This cyanine dye completely inhibited the growth of *Lactobacillus casei* at 2×10^{-6} M. *L. arabinosus* was inhibited by a concentration of 2×10^{-6} M, *Streptococcus faecalis* by 4×10^{-6} M, and *Escherichia coli* by 3×10^{-6} M. The inhibition of *E. coli* by 3×10^{-6} M concentration of cyanine dye was partially reversed by 100 mg./100 cc. of vitamins B_1 and B_2, nicotinic acid, and pantothenic acid. The reversal by crude yeast and liver extracts was even greater than indicated by their vitamin content. Vitamin B_6 and p-aminobenzoic acid were without effect on the inhibitory action of the dye.

In order to determine the nature of the bacterial inhibition, the effect of the cyanines on various enzyme systems was studied. There was no appreciable effect on the d-amino acid oxidase, cytochrome oxidase-cytochrome C, succinic dehydrogenase, glucose dehydrogenase, lactic dehydrogenase, and liver glyoxalase enzyme systems.

Representative dyes were also tested *in vivo* for activity against *Str. hemolyticus*, *Str. viridans*, *Staph. aureus*, *Diplococcus pneumoniae I*, *Trypanosoma equiperdum*, *Treponema pallidum*, St. Louis encephalitis, influenza, typhus, and other viruses, and a group of intestinal parasites; also *in vitro* against *Endamoeba histolytica*.[3] While an occasional compound showed some demonstrable activity against these organisms, the order of activity was not sufficiently great to be therapeutically significant.

A summary of the cyanine, styryl, and related dyes studied will be supplied on request.

[1] The dye syntheses were carried out by E. Van Lare, R. H. Sprague, F. L. White, G. H. Keyes, and Miss G. VanZandt, to whom the authors acknowledge their indebtedness.

[2] These investigations will be reported at the May meeting of the Federated Biological Societies in Chicago by R. N. Bieter and A. D. Welch and their associates.

[3] The authors acknowledge the work of F. D. Stimpert, O. M. Gruhzit, O. D. Bird, and G. Rodney, of the Research Laboratories, Parke, Davis & Company, under whose supervision many of these tests were performed.

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Hereditary Obesity and Efficient Food Utilization in Mice[1]

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Energy costs of transferring food materials into body tissues constitute a recurrent problem of genetics, nutrition, and physiology. The specific problem of inherited fatness in relation to efficiency of food utilization came to our immediate attention in a study of rate and economy of gain and carcass composition of swine (*3*). It was found that the hereditary influences which reduced the food required per pound of gain also increased the proportion of the gain that was fatty tissue. These results were at variance with the supposition that food requirements would be larger for deposition of fatty tissue, because of its higher energy content, compared with nonfatty tissue. This supposition apparently holds for the

[1] Journal paper No. J-1422 of the Iowa Agricultural Experiment Station, Ames, Iowa; Project No. 252.

This work was aided by a grant from the Rockefeller Foundation.

increase in fat deposition during the later stages of development of a given animal. However, we were concerned with the effect of hereditary differences in the composition of weight gains on food required per unit of gain among different animals at a similar stage of growth. This may involve heritable differences in food consumption and in energy expended for activity and other body work, as well as differences between fat, carbohydrate (*5*), and protein in the energy required for transfer from food to body tissue.

Because of certain limitations of the swine data and the broad implications of the findings, it became desirable to study more critically the nature of inherited fatness in relation to food utilization. The marked adiposity induced in mice by the "yellow" gene (*2*) seemed to offer unusual opportunity for the controlled experiment (*4*) which is reported briefly here.

Because yellow coat color in the mouse is produced by a dominant autosomal gene in the heterozygous condition, crosses to nonyellow mice give approximately equal numbers of yellow and nonyellow progeny within each sex. Accordingly, yellow and black agouti segregates were obtained by crossing yellow males of a highly inbred stock, kindly provided by L. C. Dunn, with albino females of another highly inbred

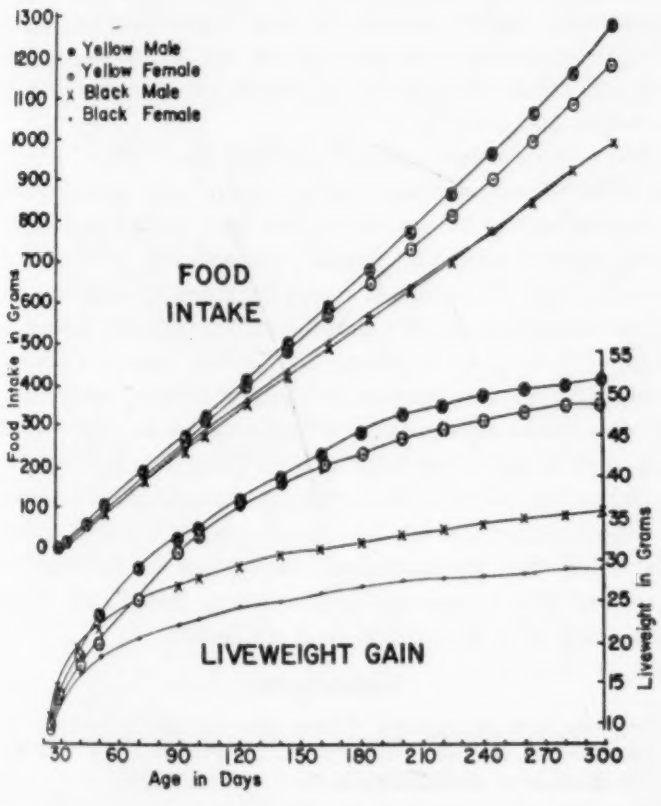

FIG. 1

line of our own. The yellow and black littermates of the same sex differed presumably only in the one chromosome or portion thereof which carried the "yellow" gene. Sets of unmated yellow and black littermates were compared within each sex and growth period, the periods being from 25 days to 30, 50, 90, 200, and 300 days of age. Each such series of comparisons was replicated four times, at approximately monthly intervals, to measure seasonal and litter variation in the results. A total of 62 yellow and 65 black mice were used. The mice were self-fed in individual cages to permit full expression of genetic differences in appetite as well as in utilization of food consumed. The only food was a complete, finely ground ration fed in shallow jelly glasses with access through a hole in the cover. The shelves containing the feeding cages were completely enclosed by fine screen to prevent food loss to stray mice. Feces, urine, and spilled food were recovered on waterproofed paper trays. Live weight gains, food consumption, and feces production were obtained by 10-day periods from 30 to 50 days and by 20-day periods thereafter. At the close of its feeding period each mouse was chloroformed, and its whole body was analyzed for fat, nitrogen, water, and total dry matter by Prof. Wilkinson, of our Experiment Station chemistry staff. Body composition was also obtained for yellow and black mice from two litters within each sex at 25 days of age.

The curves in Fig. 1 show the average gain and food consumption for all sets of yellow and black littermates within each sex and age. From 25 to 35 or 40 days of age, yellow and black mice of the same sex were nearly alike in both gain and food consumption, and the gain was predominantly protein. After 40 days, yellow mice of both sexes exceeded their black littermates greatly in gains but only moderately in food consumption. It is evident from Fig. 2 that the extra gain of the yellow mice was entirely fat tissue. Hence, it is immediately clear that the "yellow" gene greatly increases the energy stored per gram of gain but at the same time sharply reduces the food required per gram (and even more so per calorie) of gain. For example, during the period from

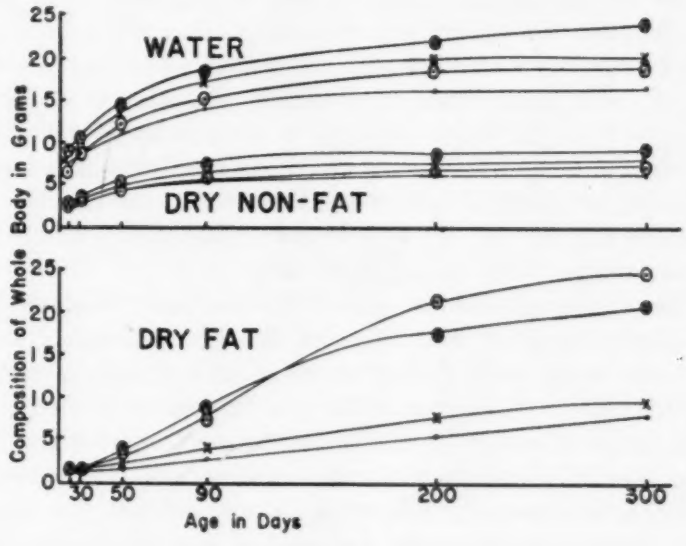

FIG. 2

40 to 90 days of age, food requirements per gram of gain were only .44 as much for yellow as for black females and .66 as much for yellow as for black males. The greater efficiency of the yellow mice is even more pronounced when the comparison is made from weaning to a fixed final weight, so that the faster gain of the yellows directly reduces the number of days fed. For example, from 25 days to a final weight of 25 grams in females and 30 grams in males, the ratios of food consumed per gram of gain by yellow to that by black mice were .38 in females and .51 in males.

The yellow gene accomplished the increased fat deposition and the lowered food requirement per unit of gain by increasing the appetite slightly and reducing the energy expended in body work, especially in activity, beginning at 35 or 40 days of age. Rytand (*9*) also observed this increased appetite of

yellow mice. Judging by the weights and average composition of feces, the percentage of the food calories eliminated in the feces (and in the urine absorbed by the feces) ranged from about 19 in the 25–30–day period to about 23 in the 25–300–day period. It was slightly lower for black females than for the other three groups, perhaps because more urine was absorbed by spilled food and less by feces for the former. Thus, the increase in nutrients absorbed by yellow, as compared with black, mice was nearly in proportion to the increase in food consumption. Furthermore, the increase in energy expended in body work by the yellow mice was proportionally much less than the increase in their average body weight, particularly in females. For example, the increase of yellow over black mice in calories absorbed from 25 to 300 days of age was 20 per cent in females and 34 per cent in males, whereas the increase in calories stored in the body was 210 and 114 per cent, respectively. Energy used for body work (food less feces and gains) increased only 15 per cent in females and 32 per cent in males compared with increases of 56 and 39 per cent, respectively, in average body weight for the period. Taking calculated energy expended in body work per unit of average body weight as 1.00 for black females, relative values for black males and for yellow females and males were .82, .74, and .78, respectively. Similar results were obtained during periods when mature mice (usually over 180 days of age) made little or no change in weight. Here it was found that food requirements per gram of body weight were only .75 as large for yellow females and males and .87 as large for black males as those for black females. These results corresponded with our observation throughout the experiment, that black females were much more excitable and active than yellow females or males, with black males intermediate. The amount of food thrown from the dishes provided a crude index of activity. Limited observations on mature mice indicated that daily food spillage per gram of body weight was 1.3 grams for black females but only .20, .05, and .17 gram, respectively, for black males and for yellow females and males.

The data emphasize how little of the food energy is stored in the body compared with that used for the maintenance and activity of the body. Energy stored as fat and protein represented only 2–11 per cent of the total food energy during the several periods from 25 to 300 days of age, whereas energy expended in body work represented 70–80 per cent. Of the total calories consumed, the yellow mice stored 2–5 per cent more than their black littermates and used at least that much less for body maintenance and activity. A relatively small reduction in maintenance food thus causes a large increase in food stored.

The work of Miss Weitze (*11*) has only recently come to our attention. Her results agree closely with ours with respect to the effect of the "yellow" gene on the rate and composition of gain and on appetite. However, she found no effect on activity as measured by a treadmill or on food energy used for maintenance and activity per unit of body weight. These discrepancies may be due to inadequacy of a treadmill for measuring natural activity and to the fact that metabolism data was obtained for only one yellow mouse of each sex, using average figures for composition of the gains. Her results from parabiosis, hypophysectomy, and histological studies indicate that the action of the "yellow" gene is hormonal, involving altered carbohydrate metabolism.

There is evidence that the action of the "yellow" gene is similar to that of the genes affecting fat deposition in animals generally. Recent correspondence with Miss Kennedy indicates that the strain of rats produced at the Minnesota station (*7*) by selecting for efficient food utilization gained more rapidly and required about 30 per cent less food per gram of gain and unit of body weight than the strain selected for inefficient gains, under full feeding. The extra gain of the "efficient" strain was largely fat tissue. Further evidence is provided by MacArthur's (*6*) selection for slow and for rapid growth to 60 days of age in two strains of mice. After 8 generations, mice of one strain were twice as large as those of the other, and mice of the large strain "tend to become sluggish and obese," whereas mice of the small strain "are very active and aggressive," suggesting a difference in metabolic rate. Differences in activity rather than in resting metabolism are indicated by Benedict's (*1*) finding that the heat production of resting mature mice per unit of calculated surface area ($\frac{2}{3}$ power of weight) was the same for an exceedingly fat race (MacDowell's CHS Silvers, not "yellows") as for common laboratory and wild mice. Salcedo (*10*) found that mice of this same fat race oxidized tissue fat more slowly than normal mice when starved and interpreted this slower fat oxidation by the fat race as the cause of their obesity. However, both could be the result of inherently smaller energy requirements. Ritzman and Colovos (*8*) have shown how strikingly the genetic association of fatness with efficient gains is exemplified in the pig, as contrasted with sheep and cattle, because of its greater appetite and reduced heat losses and activity.

The evidence presented indicates that the "yellow" gene in mice reduces food requirements per unit of gain and produces obesity, primarily by increasing the food intake and by reducing energy expended, especially for activity. Both of these effects increase the energy available for storage as fat, whereas the first raises only slightly, and the second reduces, the energy dissipated in body work. Hence, the "yellow" gene causes gain in weight to increase much more than total food consumption, even though the extra gain is fat tissue containing more energy per unit of weight than other tissues. These results emphasize the distinction between the hereditary association of increased fat deposition with lower food requirements per unit gain in weight and the developmental association of increased fat deposition with higher food requirements. Hereditary obesity is the result of more efficient food utilization.

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A Serological Study of Influenzal Antibodies[1]

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The purpose of this preliminary report is to give the data obtained from a survey of a population for antibodies to the influenzal agents A, B, and swine. These studies were initiated in order to ascertain the type of influenza strain that would manifest itself in the anticipated epidemic. That an epidemic of influenza was probable was dependent upon the findings that epidemics usually occur in cycles (*1*). The possibility of this epidemic being due to influenza B appeared remote in view of these cycles and past findings (*2, 3*). The consensus was that if an epidemic occurred, it would be due to influenza A.

MATERIALS AND METHODS

The strains and method of growth of these viruses[2] were the same as those described in a previous report (*3*).

One hundred random specimens of serum were taken from the serological service each week, starting the first week in September 1946. The original blood samples from which these sera were obtained were submitted to the Bureau of Laboratories for routine serological tests for syphilis.

Our procedure for the Hirst test was that suggested by Salk (*4*), but only three dilutions of the serum were tested. The sera were diluted in saline to make initial dilutions of 1:100, 1:500, and 1:1,000. To 0.5 ml. of serum dilution, 0.5 ml. of virus dilution (4 units) was added. To this mixture, 1.0 ml. of chicken erythrocytes (1 per cent) was added, and the test read after 75 minutes at room temperature. The presence or absence of a "button" was used to denote inhibition or agglutination.

RESULTS

Titrations of the sera obtained during September showed a rather high percentage of antibodies for influenza B, especially in the lower dilution. This level gradually decreased until it approximated the influenza A and swine influenza levels. There was little evidence of any antibody changes until the middle of December. A significant change then became apparent, with a steady increase in the number of individuals having antibodies to the swine virus. This increase was first noticed in the 1:400 dilutions of sera. Significant increases in dilutions 1:2,000 and 1:4,000 were not apparent until the middle of January. At this time, every serum tested showed at least a 1:400 antibody titer.

Fig. 1 shows this increase in antibodies among the population. Only that portion of the graph pertinent to the critical period is given here. It appears quite evident that the population in general has responded with antibodies specific for the swine virus. The determination of the cause for this increase in antibodies is difficult. At the time of this antibody increase there was no evidence of clinical epidemic influenza, a condition which still exists. Several volunteers donated blood samples, and the majority of these demonstrated titers above a final serum dilution of 1:2,000. There did not appear to be any relationship between the titers for the swine virus and a history of vaccination with commercial influenza A and B vaccine.

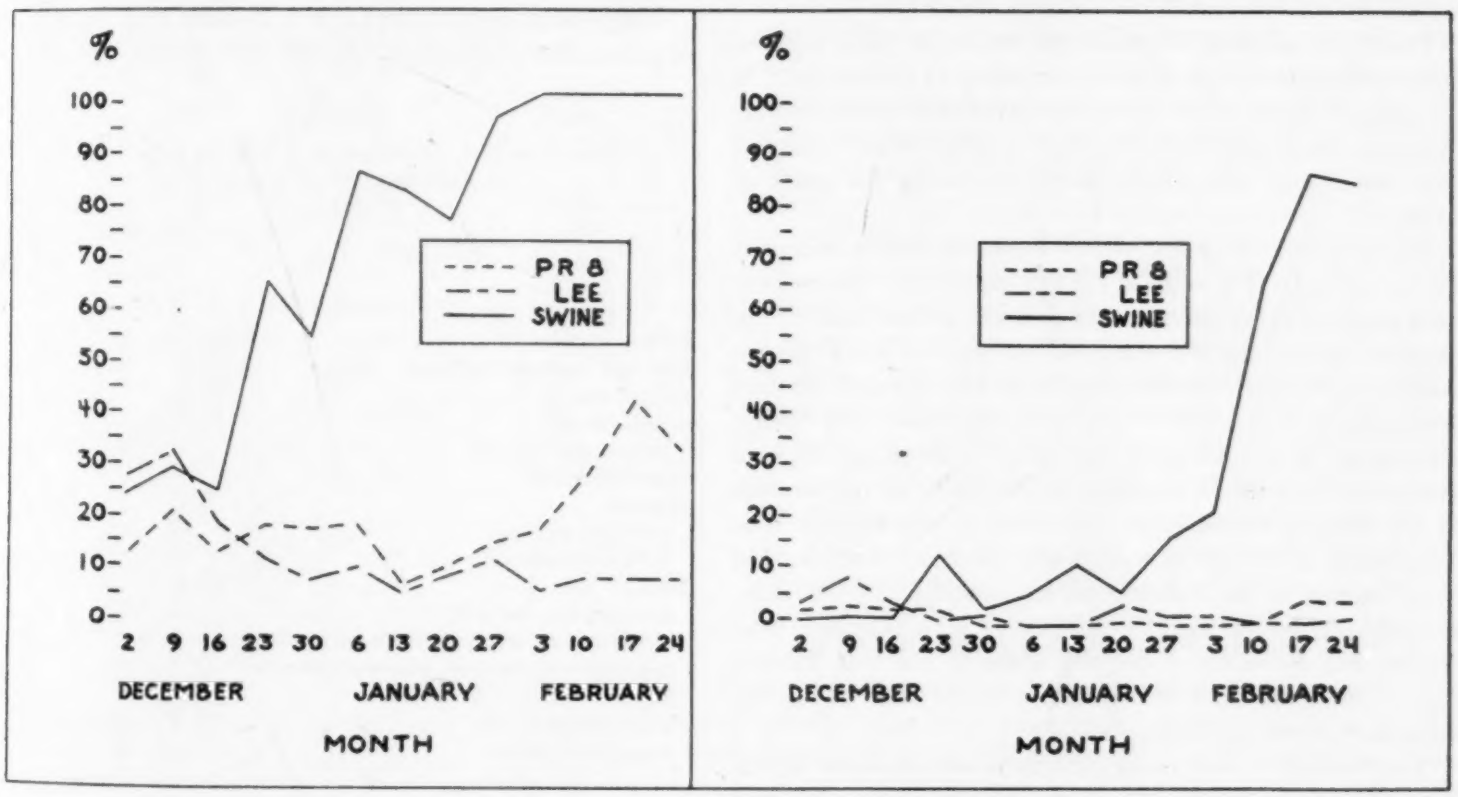

FIG. 1. Percentage sera with titers of 400 and 4,000 (final dilutions).

DISCUSSION

The results were quite unexpected. Studies of the relationship of this swine virus to strains of influenza A and to man are now in progress. Clinically, there was no evidence of epidemic influenza in this area. The only apparent evidence of

[1] Aided by a grant from the Hendricks Research Fund.

[2] The PR8 and Lee strains were supplied by Dr. Werner Henle; the swine strain, by Dr. Gilbert Dalldorf.

infection in the population, concurrent with the antibody increase, was a marked increase in apparently typical coryza.

It is realized that controls in a study of this sort are difficult. At present we are engaged in studies on sera that had been collected before and after this increase in antibodies became apparent. In addition, throat washings have been obtained from several individuals with this antibody increase, and attempts at virus isolation are being made.

Addendum: Since submission of this report an epidemic of influenza has occurred in this area. Studies are now in progress as to the etiology of this epidemic and its relationship to the above findings.

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A Bacterial Disease of the Lobster (*Homarus americanus*)

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U. S. Fish and Wildlife Service, Kearneysville, West Virginia, and *Boothbay Harbor, Maine*

During the summer of 1946 lobster dealers in Maine suffered considerable losses due to heavy mortality of lobsters held in pounds and tanks. A spot survey indicated that losses attributable to a new disease varied from 20 to about 50 per cent and that the disease was widely distributed along the coast of Maine.

It was suspected at first that these losses might be caused by the use of DDT in some of the fish canneries. Some of the offal from the canneries, which is used as bait and food for the captive lobsters, might contain toxic amounts of DDT. Microscopic and bacteriologic examination of the diseased lobsters indicated, however, that it was more likely that the disease was caused by a bacterium belonging to the genus *Gaffkya*. Wherever there was a considerable mortality of the lobsters at the time of examination, micrococci of the *Gaffkya* type were found in the blood smears and the blood culture. The blood needed for the microscopic examination and for isolation of bacteriologic media was removed by a puncture from the ventral abdominal sinus with a sharp, pointed, Pasteur pipette following surface disinfection of the thin membrane between the somites of the abdomen.

The diseased lobsters had a pink discoloration of the ventral side of the abdomen; the blood was also pink, less viscid, and usually with much-prolonged clotting time. In advanced cases, in which there was a large number of bacteria in the blood stream, the number of blood corpuscles was sharply reduced.

The severity of the disease appeared to be decreasing with the onset of colder weather. At certain pounds the infected lobsters predominated in September, but in October they could not be found in the same pounds. However, an outbreak of the disease with typical symptoms, high mortality and the presence of *Gaffkya*, was reported in December.

The organism, which was regularly isolated from diseased lobsters in pure culture, could be grown fairly easily on the standard media. Solid and semisolid media prepared with the tryptic digest of casein and yeast extract gave very satisfactory results. On these the growth was reliable, but the amount of growth was always small. Colonies about 1 mm. in diameter, circular, convex, and grayish-white, were produced. In semisolid and liquid media scant granular sediment was produced. The organism neither changed litmus milk nor liquefied gelatin. It produced acid, but no gas, from mannitol, dextrose, sucrose, maltose, and lactose.[1]

In the fresh blood of the infected lobsters the organism was found to be present in tetrads surrounded by a wide pseudocapsule around the group. In media it produced irregular conglomerations without capsules. In stained preparations it was gram positive. It was also nonmotile.

A series of lobsters was inoculated intramuscularly and intravenously with the pure cultures of this microorganism. All inoculated lobsters died within two weeks with the typical symptoms of the disease, and from the blood of these lobsters the organism was reisolated in pure culture.

Two randomized experiments were made on the effect of the inoculation of normal lobsters and on the treatment of infected lobsters with sulfonamides, which have been found effective against some bacterial diseases of fishes (*1*). The lobsters were distributed, two to a tank, in randomized blocks. They were fed ground herring or redfish mixed with gelatin, to which sulfonamides or bacteria were added. Some were fed infected lobster.

The results, compiled in Table 1, indicate that the injection of pure culture of *Gaffkya*, isolated from diseased lobsters, invariably killed the lobsters within two weeks, even if they were treated with sulfonamides. Introduction of bacteria with food was ineffective, and sulfonamides seemed to reduce the mortality only among the lobsters which contracted the disease in a natural way.

TABLE 1

The Effect of Artificial Infection of Lobsters and of Treatment With Sulfonamides

Treatment	Initial No. of lobsters	No. 2 mortalities
Normal controls	30	2
Diet with bacteria (*Gaffkya*)	30	4
Normal controls		
Sulfamerazine	10	1
Sulfamethazine diet	10	1
Diseased controls	10	5
Diseased		
Sulfamerazine diet	10	1
Sulfamethazine diet	10	1
Normal		
Injected with bacteria	30	29
Injected with bacteria, sulfamerazine diet	10	10
Injected with bacteria, sulfamethazine diet	10	10
Injected with sterile medium	20	2
Fed infected lobster	10	1
Fed normal lobster	10	1

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[1] Detailed study of the organism is in progress at the Department of Bacteriology, University of Maine; the results will be published elsewhere.

IN THE LABORATORY

Improved Electrophoresis Cell and Cell Holder

STANLEY M. SWINGLE

Gates and Crellin Laboratories of Chemistry,[1]
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Those laboratories fortunate enough to possess a Tiselius electrophoresis apparatus frequently accumulate more work than they can handle because of the length of time required for each determination. Unless the cells are cleaned frequently and the sliding joints regreased, experiments may be spoiled by the development of leaks between the sections or at the neoprene connections with the electrode vessels. Much time may be saved by using a pair of the cells and cell holders, as shown in Fig. 1,

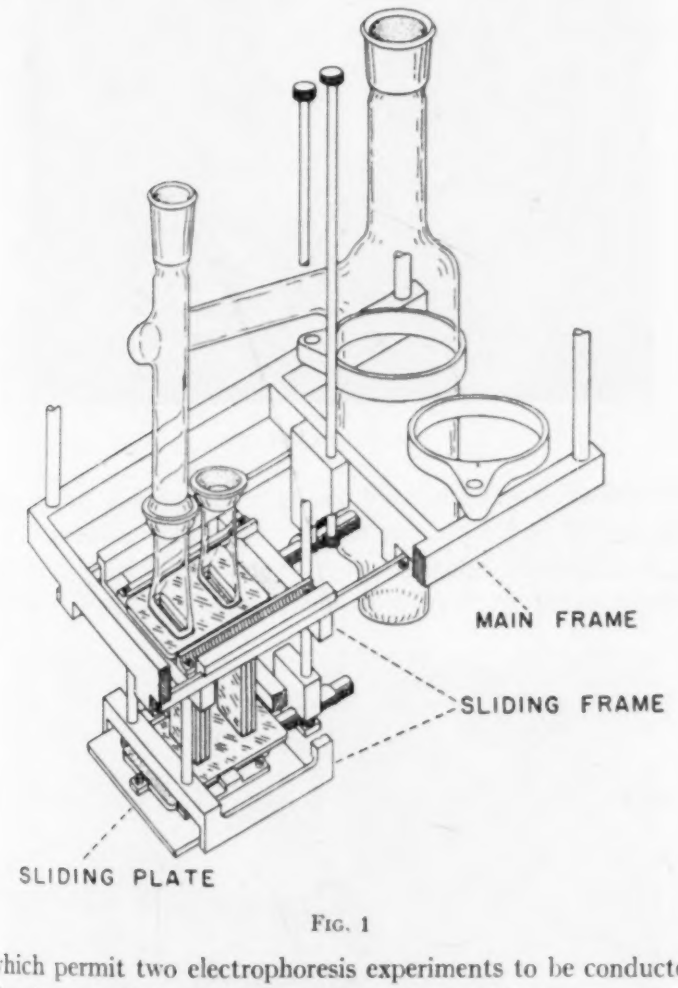

FIG. 1

which permit two electrophoresis experiments to be conducted simultaneously in one apparatus with a minimum of trouble from leakage. The double-length cells described by Longsworth, Cannan, and MacInnes (*1*) are particularly easy to manipulate for filling in this cell holder, and the danger of breakage is eliminated because the force required to slide the joints is applied directly at the edges of the sliding glass plates.

The main frame of the cell holder carries a smaller sliding frame in which are held both the middle section of the cell and a device for manipulating the bottom section. When the right-hand knob at the top is turned, the corresponding rack and pinion move this sliding frame, thus opening or closing the connection between the middle and top sections without, however, affecting the lower joint. The top section is held in place by a removable holder (not shown) on the main frame, which has projections to locate the glass plate by the edges and springs to press the sliding joint together. Similarly, the left-hand knob and a second rack and pinion mounted on the sliding frame move a sliding plate in which is held the bottom section, thus operating the lower joint without affecting the top joint. This is in contrast to the operation of the usual cell holders in which a piston (*3*) or rack and pinion (*2*), by applying force near the center of the middle section, moves this section while both the top and bottom stay fixed. If the frictional forces at the two joints are not equal, the resultant torque tends to tilt the middle section and either open the joints or break the cell.

Much of the success of the new holder depends on mounting the cell so that there is no overconstraint. Attached to the sliding frame along opposite edges of the glass plates of the top joint are two guide bars, which keep the top and middle sections parallel with the frame. Six additional points of contact between the middle section and the sliding frame are provided by buttons (not shown) located at the midpoints of the two remaining edges of the top glass plate and the four edges of the bottom plate. Thus, the middle section is fixed and strain free relative to the sliding frame, except that it can move vertically to make contact with the bottom section. The bottom section is held in the bottom sliding plate which maintains alignment with the middle. This sliding plate, which holds the entire weight of the cell as well as the force of the springs on the top section, rides on a single point at its center so that the pressure between the sections of the cell is uniformly distributed over the entire area of the sliding joints. In the usual type of cell holder, the weight is carried by guides at both sides of the bottom, with the result that, unless the frame and cell conform exactly, the weight is actually carried at only one edge, and the bottom joint is held together only by the cohesion of the grease. Leakage usually develops after the joint has been slid only a few times. The use of such a one-point support in other types of holder or simple cushioning of the bottom section on soft rubber, as suggested by Svensson (*3*), would probably help. With the new holder, leakage has never been observed. Even after 20 consecutive runs on one occasion, there was no obvious leak, although the delicate test of electrical leakage was not applied.

The arrangement of the spherical glass connection with the electrode vessels is apparent from Fig. 1. In order that the joints may be assembled without strain, each electrode vessel is mounted with some freedom in a sling (not shown) under the ring holding the vessel to the main frame. This ring, in turn, is pivoted to allow some horizontal motion. By mounting both electrode vessels on the same side of the cell, two complete units can be put simultaneously in the thermostat bath with the cells adjacent. The frames are supported from the top on a track across

[1] Contribution No. 1120.

the tank so that either cell may be rolled into position in front of the windows for observation. Spherical joints can be added to pre-existing equipment if the supports for the electrode vessels are given slight horizontal freedom. A method for making cells has been published (*5*). Pyrex glass plates, of course, must be used for cementing to the spherical joints.

The cells and holders have been used successfully for several years in an electrophoresis apparatus using parabolic mirrors in the optical system, as described elsewhere (*4*).

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Administration of Micronized Therapeutic Agents by Inhalation or Topical Application

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There are many disadvantages to the present method of administering therapeutic agents by the aerosol principle. The major objections are: (1) the wasteful, expensive, and unnecessary use of oxygen merely as a source of pressure; (2) the fact that the manual methods are time consuming and tiring (20–30 minutes/dose); and (3) the fact that the penicillin solutions used deteriorate rapidly and must be kept refrigerated to retain full potency for one week.

A small ball mill (Fig. 1) has been built, using readily available materials, which will grind various therapeutic agents to a micronized state in two hours. The material is then bolted through fine-meshed silk bolting cloth. When 40–50 grams of the mixture is prepared by use of this apparatus, the loss is less than 10 per cent.

Several modifications of the apparatus for administration of the smoke have been devised. The final apparatus is shown in Fig. 2. The lower chamber contains drierite, which is a dehydrating substance (anhydrous calcium sulfate), with an indicator which turns from blue to pink when it has picked up all the moisture it can. The lower chamber is filtered on both ends to prevent the drierite from being blown into the smoke-producing chamber or from being drawn into the air-intake opening. The smoke chamber has been built with a small surface area to increase the emptying efficiency. The air vents into this compartment are placed at an acute angle to force the powder into a spiral path in order to create turbulence. The outlet tube is likewise made of small internal caliber to reduce the amount of precipitate on the walls of the tube. Various adapters (nasal, oral, dental, vaginal, etc.) can be fitted to the outlet tube. This equipment can be used as it stands or fitted with a rubber mouthpiece. In other words, no bulb is necessary, but the exit tube or rubber mouthpiece can be placed in the mouth, and, by inhaling through the apparatus, the finely divided therapeutic agents can be drawn into the lungs. Efficiency studies indicate that, when used correctly, the apparatus will deliver in the smoke form 95 per cent of the

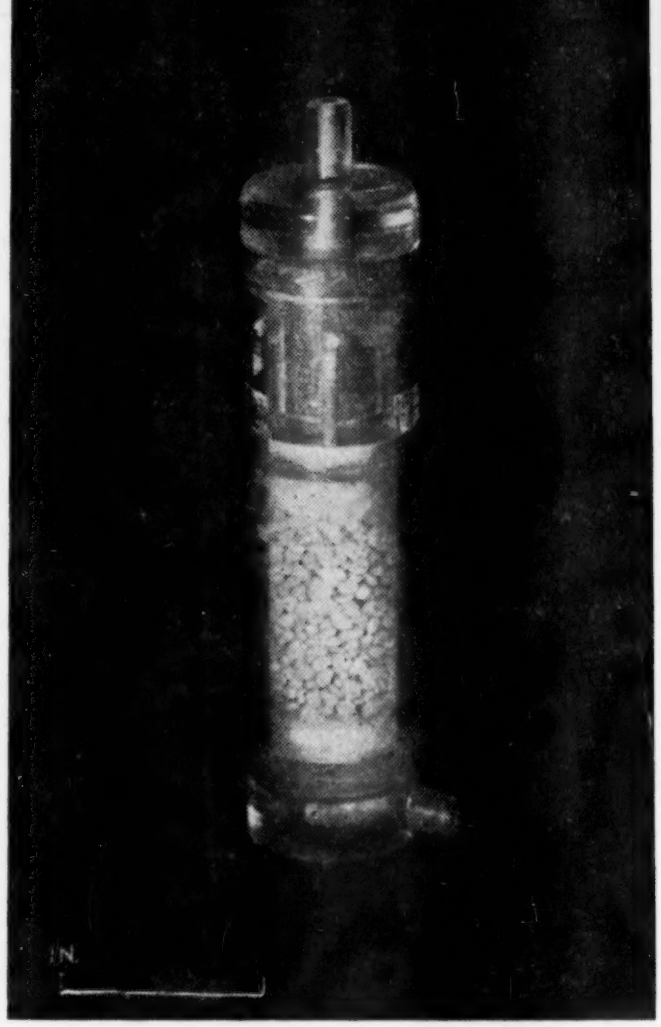

Fig. 1. The ball mill.

therapeutic agent originally placed in the cup and may be administered by the patient in from two to four minutes.

A disposable apparatus containing the principles of the smoke chamber may be molded very inexpensively by the

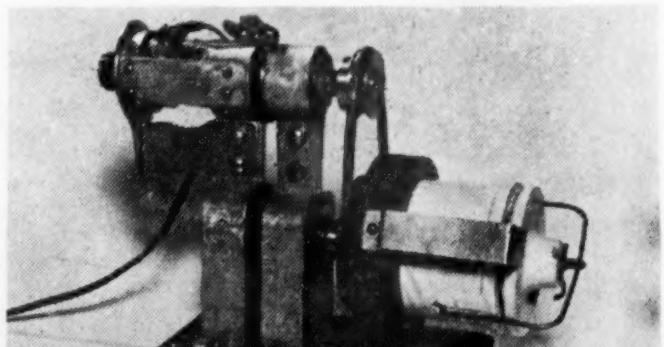

Fig. 2. The apparatus.

use of one of the transparent plastics. This apparatus may be used as both container and dispenser for the penicillin or other therapeutic agents.

Blood penicillin concentrations were determined by the

method described by Wolahan and Cutting (*1*). Results on the blood levels in subjects inhaling various doses of the micronized potassium penicillin-glucose preparation are shown in Table 1.

TABLE 1

Patient	Dosage (units of crystalline penicillin)	Interval after administration	Concentration (units/cc. citrated whole blood)
C*	30,000	½ hr.	.03
		1 "	.03
T*	30,000	½ "	.06
		1 "	.03
R*	50,000	½ "	.03
		1 "	.03
		2 "	.015
S*	50,000	½ "	.06
		1 "	.03
		2 "	.03
		3 "	.03
L	25,000	½ "	.015
		1 "	.015
		2 "	.015
M	30,000	1 " 20 min.	.06
		2 "	.06
P	30,000	1 "	.06
		2 "	.03
B	160,000	1 "	.06
		2 "	.03
		4 "	.03
		6 "	.03
		8 "	.03
		10 "	.03
		12 "	.00
O'N	90,000	½ "	.125
		1 "	.06
		2 "	.06
		3 "	.03
		4 "	.06
H	90,000	½ "	2.000
		1 "	.125
		2 "	.125
		3 "	1.000 (?)
		4 "	.060
		5 "	.060

* Normal controls. Penicillin and penicillinase controls were performed.

In all cases except one (L) where 25,000 units or more were administered, a therapeutic concentration was obtained in ½ hour and maintained for about 3 hours. After large doses (B and O'N) the therapeutic levels are maintained for approximately 10 hours. In two cases studied it was found that 10–15 per cent of the dose administered was excreted in the urine in the first hour.

Any soluble therapeutic agent which can be produced in the solid state or which can be chemically precipitated or physically combined with glucose, β-lactose, lactose, etc. may be micronized and used in the manner described. Some of the agents meeting these requirements are: the sulfonamides; antibiotic agents such as penicillin and streptomycin; hormones such as insulin and estrone; antihistamine drugs such as Benadryl; vasoconstrictors such as neosynephrine and ephedrine; narcotics such as codeine and dilaudid; biologicals such as immune human globulin, vaccines, etc.; various medicinal compounds such as cough mixtures; and numerous others. These materials may be used individually or in compatible combinations, with or without a vehicle.

In certain diseases principally those in which a high local concentration of the agent at site of the infection or reacting organ is of great importance, this method of therapeutics is particularly advantageous. These include certain diseases of the respiratory tract, topical application where indicated, allergic states, and urinary tract infections. The method is also useful in the prophylaxis of venereal diseases, acute rheumatic fever, common carrier states, and the prevention of postoperative pulmonary infections.

This method of administering penicillin glucose mixtures has been used in more than 40 cases of various diseases where penicillin therapy was indicated. The clinical and bacteriological response to treatment has been excellent. Patients prefer this type of treatment to injections or aerosol. By the incorporation of from 2 to 5 mg. of Benadryl/dose of penicillin glucose mixture (200 mg.) there have been no local sensitivity reactions to penicillin in the last 35 cases.

This preliminary report is presented for the purpose of stimulating further study of the method described. Several studies of the suggested applications of the method are in progress at the University of Rochester School of Medicine and Dentistry by members of various departments of the University.

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A Simple Device to Increase Background Contrast in Photomicrography

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In the photography of small insects it has been considered necessary in this laboratory to find a means of intensifying the blackness of the background. A simple microscope attachment was therefore constructed to make possible the desired contrast between the photographed object and the background. This device, which is essentially the physicists' "black body," consists of a cavity with a small opening and with interior walls of low reflectance. The opening is placed beneath the specimen to be photographed and provides a background of very nearly zero reflectance, since the light that enters the opening is absorbed within the cavity.

To construct this cavity, it was found convenient to use the black bakelite cover of a microtessar lens container, but any cylinder of comparable dimensions and lined with a nonreflective black substance should be satisfactory. A disk of black photographic paper with a ¼-inch hole cut in its center was glued over the open end to provide the small opening referred to above. This simple device will ride on the condenser lens and can be elevated into position immediately below the

[1] The writer wishes to thank R. E. Worley, of the Physics Department at this University, for his review and criticism of this paper.

microscope slide holding the specimen. A felt pad attached to the bottom of the device will eliminate the possibility of scratching the condenser lens.

With the ¼-inch hole in position beneath the specimen, a deep black background is provided even when the specimen is strongly illuminated with flood lamps. Thus, in the case of predominantly "black" insects, sufficient contrast is provided between the reflective "black" of the insect and the nonreflective black of the background formed by the cavity.

As it was constructed, the device (Fig. 1) is 1¼ inch in diameter and has a depth of ¾ inch. However, the use of any

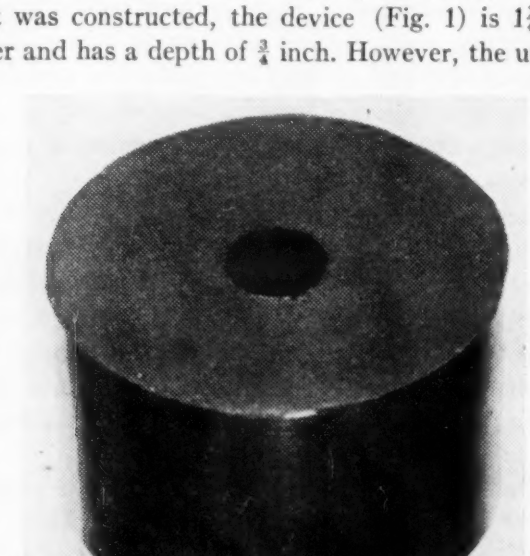

FIG. 1

properly blackened box with flat, removable lids having various hole sizes will serve a similar purpose when objects of greater dimensions are to be photographed.

Crystalline Dihydrate of Calcium Ascorbate

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Szent-Györgyi (*3*), in investigating vitamin C, mentioned that the solubility of the calcium salt excluded its identity with that of the acid studied by Bertrand and others.

Hirst, *et al.* (*1*) prepared the calcium salt by adding a slight excess of calcium carbonate to the aqueous solution of ascorbic acid. The solution was evaporated to dryness in a desiccator. The dry residue was then triturated with alcohol when a neutral salt was obtained which had a pale yellow color and gave an aqueous solution with a rotation of $[\alpha]_D^{19} + 91$. Analysis showed a calcium content of 9.9 per cent, as compared with the theoretical 10.2 per cent, for $(C_6H_7O_6)_2$. No analysis of the carbon or hydrogen was stated, and apparently the substance was not crystalline.

Calcium ascorbate, prepared as a cream-colored dry powder, has been made in considerable quantites for medicinal preparations. However, because of its hygroscopic property, this soon took up moisture when exposed to a humid atmosphere and became gummy, decomposing to an orange-colored product. It was thus unsuitable for practical use.

One of the writers (S. L. R.) developed the stabilized solutions of calcium ascorbate which have since been widely used. Study was continued, however, to secure a stable, dry form of calcium ascorbate that could be employed for oral therapy. This has apparently been attained in the dihydrate of calcium ascorbate.

While investigating the production of a more stable form of calcium ascorbate we have succeeded in crystallizing this important salt from water. The crystals obtained are white, are much more stable than the uncrystallized salt, and have remained dry and white when exposed for several months to the humid atmosphere of the laboratory.

Due to the known tendency of ascorbic acid solutions to oxidize and undergo further decomposition, solutions of the calcium ascorbate were were not allowed to stand for long periods in water or alcohol, nor was the temperature of the solutions allowed to rise much above 30°. It was found necessary to dry the crystals with absolute alcohol and to remove the alcohol quickly to avoid oxidation of the crystals, with subsequent coloration.

METHOD

The first product to approach the crystalline salt in composition was obtained by precipitation in acetone. Sixty grams of ascorbic acid was dissolved in 140 cc. of hot water, the solution cooled to 30°, and 16.3 grams (a little less than ½ mole) of calcium carbonate added slowly with stirring. The solution was filtered with suction to remove a small residue and the excess of carbon dioxide. The aqueous solution was run in a thin stream by means of a pipette into 3,000 cc. of acetone with constant stirring. Some gum, in addition to a flocculent precipitate which at first was in suspension, formed on the bottom of the beaker. The gum was kneaded with the stirring rod and, on standing overnight, became brittle. This was broken up, the acetone decanted, and the precipitate washed with 300 cc. of fresh acetone. The material was filtered, ground in a mortar, rubbed up in about 200 cc. of ether to remove the excess of acetone, and filtered with suction to remove ether. When dry, it contained 9.3 per cent calcium.

One gram of the calcium ascorbate obtained by precipitation from acetone was rubbed up in 0.5 cc. of water. Crystals formed which, under the microscope, appeared as prisms.

Crystalline calcium ascorbate was next prepared from water, using as seed the first crystals obtained. One hundred and twenty grams of ascorbic acid was dissolved in 280 cc. of hot water, the solution cooled to about 25°, and 32.6 grams (a little less than ½ mole) of calcium carbonate added with stirring. The solution was filtered with suction, as before, to remove the small residue and excess carbon dioxide, and the filtrate was evaporated *in vacuo* to a thin syrup of about 170-cc. volume. On seeding and stirring, a crystalline mass was obtained which, after standing no longer than an hour, was filtered with suction, the crystals then being rubbed up with 200 cc. of absolute alcohol, refiltered, and washed with an additional 50 cc. of alcohol to remove excess moisture. Alcohol was removed by drawing air through the filter and then spreading the crystals on filter paper to dry. The yield was 71.9 grams, or 49.5 per cent of the theoretical. Higher yields were obtained when the solution was evaporated to a thicker syrup.

The crystals remained white and dry for months on exposure to the humid atmosphere of the laboratory.

The analysis of these crystals indicates a calcium ascorbate dihydrate.

	Found	Calculated for $(C_6H_7O_6)_2Ca2H_2O$
Calcium	9.42	9.40
Carbon	33.48	33.81
Hydrogen	4.24	4.25

Titration of 0.4000 gram of the calcium ascorbate in 100 cc. of N/1 acetic acid solution required 37.34 cc. of N/10 iodine, giving a value of 82.15 per cent ascorbic acid (theory for the dihydrate, 82.63 per cent).

From the above analysis one may conclude that the calcium ascorbate is a dihydrate, although drying of 0.6447 gram of the substance in vacuum at the temperature of boiling toluene for 6 hours resulted in a loss of only 0.65 per cent. At this temperature a slight decomposition occurred, with the substance turning a light yellow color, and no higher temperature was attempted in drying the calcium ascorbate. It is well known, however, that many calcium salts are combined with water, which is difficult to remove, and this crystalline calcium ascorbate is undoubtedly such a hydrate.

The specific rotation of the crystalline calcium ascorbate obtained in water was $[\alpha]_D^{20} + 95.6$ (C2.4). That obtained by Hirst for his product was $[\alpha]_D^{19} + 91$.

A study of the crystallographic and optical properties of the dihydrate of calcium ascorbate was conducted by Wilbur G. Valentine.

The material consisted of two lots: a dry sample, and a supersaturated liquor in which crystals were forming. The problem was to determine the type of crystals, assign them to the proper system, and determine the optical properties in so far as a petrographic inspection would allow.

General Results

The dry sample appears to be uniform in crystallization. The crystals, which have rather definite crystal boundaries, show no evidence of deterioration on the boundaries, even after standing for a month in contact with air. In general, they are somewhat elongated triclinic crystals, with the principal optical directions oblique to all edges between crystal faces and to the general elongation of the crystals. The faces appear to be in pairs on opposite sides of the crystals.

Crystals from the concentrated liquor were also observed. In general, those forming on the sides and bottom of the vessel were larger than those in the dry sample and did not have well-formed external faces. Optically, they behaved in the same manner as those from the dry sample and are assumed to have the same triclinic crystallization. A thin skin of crystals also formed on top of the liquid. A short examination of these crystals showed that they are quite different from the others. They are distinctly elongated, being 5 to 10 times as long as they are wide. The cross-section of the prismatic crystals appears to be square. If this is true, they are almost certainly tetragonal in crystallization. The terminations are usually simple pinacoids, but partly developed pyramids were noted in a few instances.

Optical Properties

Triclinic form. In most cases the greater index vibration direction was across the crystal, and the lesser more nearly parallel to the direction of elongation. In some instances, however, this situation is reversed. Hence, the elongation of the mineral is more nearly parallel to the vibration direction of the intermediate index, β. The greatest dimension perpendicular to the elongation is closest to the vibration direction of the greatest index, γ, and the shortest dimension is most nearly parallel to the vibration direction of least index, α. Because of this orientation, the determination of α in the liquid media of low viscosity used in the inspection is least certain, but the determination of γ should be fairly accurate. The best determination of α is that it lies between 1.530 and 1.535 and is nearer 1.530; γ is very close to 1.680; β was not measured directly, but should lie at about the midpoint between the two extremes. The birefringence, γ-α, is 0.150. That this is very high is borne out by the high colors shown by the small crystals observed.

Many crystals give very poor optical figures because of small size and poor orientation. All figures are definitely biaxial. In all cases where the determination seemed definite, they are biaxial negative. A few optic axis figures were seen, and the isogyre has only a slight flexure in the diagnonal position. Hence, the optical angle is nearly 90°. The isogyres and color bands are sharp, indicating very little dispersion.

Tetragonal form. The study of these crystals was not extensive enough to allow as much certainty of the results as in the case of the triclinic crystals. The vibration direction of greater index is parallel to the length of the prisms and seems to be slightly higher than 1.535. The lesser index is very close to 1.530. Hence, the birefringence falls between 0.005 and 0.010. The birefringent colors check with this determination, being low gray for most crystals. No satisfactory optical figures were seen, all being flash figures. This agrees with the interpretation that these are uniaxial crystals with the C axis in the plane of the field. From the index data, the mineral should be uniaxial negative.

Other Data

The material was studied under high power with a Bausch and Lomb petrographic microscope. The mineral grains were immersed in liquid media whose indices are within 0.001 of the stated amount. The crystals of the dry sample ranged from about 0.01 to 0.05 mm. in length, and from about 0.005 to 0.03 mm. in width. The triclinic crystals from the liquor were much larger, but the tetragonal crystals were about comparable in size to the triclinic crystals from the dry sample.

X-ray diffraction studies, which were carried out by Dr. Fankuchen, showed that the material is clearly crystalline. The diagram was taken with a 57.3-mm.-radius camera with nickel-filtered copper radiation (± 1.54 A.). The spacings of the first 16 lines, shown below, are in Angstrom units:

d/n	7.20	5.73	5.38	4.82	4.67	4.19	4.05	3.92
Intensity	vs	wm	w	m	w	s	m	wm
d/n	3.72	3.49	3.27	3.15	2.99	2.95	2.79	2.71
Intensity	ms	ms	ms	m	vw	w	s	w

s = strong, m = medium, v = very, w = weak.

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Book Reviews

Nieuwe biologische Principes: Inleiding tot de Genese van de Voortplanting. (New biological principles: introduction to the genesis of propagation.) G. Wolda. 'S-Gravenhage: A. A. M. Stols, 1946. Pp. 178. (Illustrated.)

The author has collected a mass of data on the manner of propagation of birds in their natural habitat and claims to have recognized certain laws of propagation. Accepting their universal value, the author has undertaken an analysis of human propagation, which he deemed impossible without knowledge of the breeding habits of birds.

The reasoning of the author does not seem compelling, the language is not clear, and the choice of the material is arbitrary. The latter is, for instance, evidenced by the fact that the yearly death rate as well as the birth rate show certain optima. Nevertheless, only data concerning the birth rate are considered in his theories.

Not many readers will accept the new biological principles regarding the existence of phylogenetically old and new rhythms of propagation on the basis of the material presented in this book.

H. DU BUY

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Radical surgery in advanced abdominal cancer. Alexander Brunschwig. Chicago: Univ. Chicago Press, 1947. Pp. xii + 324. (Illustrated.) $7.50.

The immediate scope of this monograph is a rather limited aspect of abdominal surgery. However, broader implications are apparent on examining the rationale which led to the dramatic operations described by Prof. Brunschwig. The author feels that in recent years there has been a tendency for methods of supportive treatment of surgical patients to advance more rapidly than surgical technique. Today, surgeons may attempt to do things which would have been ill advised prior to the development of modern methods of combating shock, infection, dehydration, and starvation.

A century ago, before the advent of general anesthesia, surgery was limited to a few operations of desperation. Modern surgery was born with the successful application of anesthetic agents. More recently, other contributions to our knowledge of pharmacology and physiology have lessened the mortality and morbidity following orthodox surgical procedures. Conservative surgeons have been reluctant to exploit their new advantage with daring measures to combat diseases which, until now, have been uniformly fatal. In the field of cancer there is desperate need for improvement of cure rates as well as prolongation of life and palliation.

The text is based upon 100 consecutive cases of advanced cancer treated in the University of Chicago Clinics. The usual standards of "operability" have been disregarded for reasons which are presented in the early chapters. A major portion of the book is devoted to clinical histories and lucid detailed descriptions of operative techniques. Photographic and diagrammatic illustrations are abundant. A section devoted to supportive treatment of the surgical patient gives an excellent summary of recent developments in preoperative, operative, and postoperative care.

The last chapter consists of statistics on the cases discussed in the book. In conclusion, Prof. Brunschwig states: "The limits of operative surgery in dealing with intra-abdominal cancer are defined not in terms of operative procedures but in terms of the extent of the neoplastic process that may be encountered."

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Scientific Book Register

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